A Demographic Analysis of Primate Research in the United States

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Summary — An analysis of primate research in the USA, including the number and species of non-human primates used, types of research, levels of invasiveness, housing conditions and funding, is an important step in addressing various concerns (ethical and scientific) surrounding primate research. An analysis of monkey and chimpanzee research, conducted by The Humane Society of the United States (HSUS), demonstrated that the USA uses more non-human primates (including great apes) in research per year, than any other country in the world. The US government devotes approximately $575–800 million per year to primate research and care. Chimpanzees are most commonly used for hepatitis research; monkeys are most commonly used for HIV research, and other research areas include vaccine and drug testing, cognition, human pathologies/diseases, drug abuse and xenotransplantation. Legislation (including great ape research bans), media attention and proposed increased primate use also contribute to the overall picture of current and future non-human primate research in the USA and throughout the world. The HSUS proposes that cost–benefit analyses of non-human primate research in the USA be conducted to properly assess "value added" to relevant fields of research and whether the use of non-human primates is the only, or most effective, strategy for biomedical progress. Finally, The HSUS proposes a ban on the use of apes in research in the USA and worldwide.

Key words: *chimpanzee, legislation, monkey, primate, research.*

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Introduction

The use of non-human primates in biomedical research, particularly of great apes, raises many concerns and considerations, including the ethics and scientific value of using these animals. An up-to-date profile of primate research is essential to tackling these issues. Consequently, The Humane Society of the United States (HSUS) conducted an extensive analysis of primate research in the USA, including species used, number of animals used, fields of research, type of housing, invasiveness of research, and funding. The results of this analysis are presented here. To provide context, we also address US policies and regulations, the structure of non-human primate supply in the USA and relevant legislation and media attention.

There have been recent changes in national policy pertaining to the use of great apes in research. In 1997, Great Britain announced that it would not grant licences for great ape research, which it had not done since before 1986. In 2000, New Zealand implemented a legislative ban against great ape research — the first such legislative ban. Despite the fact that New Zealand has not used great apes in research, this change in policy sent a strong message to the rest of the world. In 2002, an amendment was made to the Dutch law on animal experiments that prohibits the use of great apes in biomedical research in The Netherlands. Also, Japan has halted invasive research on great apes, and the academic community is currently pressing for a ban as well (1).

In the USA, the *Chimpanzee Health Improvement, Maintenance, and Protection (CHIMP) Act*, which seeks to create a national sanctuary system for chimpanzees no longer used in research, became public law in 2000. A survey commissioned by The HSUS in 2002 demonstrated that 79% of the public support the creation of such a system. In September of 2002, Chimp Haven, a non-profit organisation specialising in the care of chimpanzees, was granted the National Institutes of Health (NIH) contract to run the national sanctuary system.

In addition to changes in public policy, there has been increased attention to primate research and great ape rights in the media, including such publications as *Nature* (1), *The Los Angeles Times* (2), *The Washington Post* (3), *The Wall Street Journal* (4) and *Discover Magazine* (5).

Finally, the Boyd Group, a group of diverse stakeholders in the UK committed to dialogue regarding animal research, has published a set of five papers regarding primate research, including moral status, issues concerning justification of their use and welfare considerations when they are used (6).

Background information pertaining to primate research in the USA

Non-human primates used in US-based research are covered under the *Animal Welfare Act* (AWA), which is enforced by the US Department of Agriculture (USDA). In addition to the USDA regulations and standards common to other species, such as those governing shelter, temperature, and veterinary care, there is an AWA standard pertaining to psychological well-being that applies exclusively to non-human primates. This standard (*Title 9, subchapter A, Section 3.81*) reads: "Dealers, exhibitors, and research facilities must develop, document, and follow an appropriate plan for environment enhancement adequate to promote the psychological well-being of non-human primates". The standards also indicate that the environmental enhancement plan "must include specific provisions to address the social needs of non-human primates of species known to exist in social groups in nature".

Following the issuance of standards for primate psychological well-being in 1991 and a subsequent lawsuit over the permissiveness of these standards, the USDA published a draft policy in 1999, clarifying what primate facilities are required to include in their environmental enhancement plan. However, in early 2002, the draft policy was withdrawn by the Bush administration for further review of issues such as its potential economic impact. According to USDA and NIH officials, the policy will not be moving forward but the two agencies have come to an agreement to collaborate and produce best management practices regarding psychological well-being for distribution to research institutions (information provided at the American Association of Laboratory Animal Science conference seminar on October 28, 2002).

The NIH is responsible for implementation of the Public Health Service (PHS) *Policy on Humane Care and Use of Laboratory Animals,* and thereby provides oversight to those institutions that receive government funding for animal research. Such institutions are required to follow the *Guide for the Care and Use of Laboratory Animals*, which addresses environmental enhancement for non-human primates and other species. The Guide includes guidance on social housing, space, and structural environment for non-human primates. However, it is important to emphasise that the language of this guidance is quite general in nature; and therefore, its impact on actual practices is debatable. Moreover, the NIH is not a regulatory body and therefore has no inspectorate.

National Primate Research Centers and other federally funded primate resources

The National Primate Research Centers (NPRCs), formerly known as the Regional Primate Research Centers, were established by Congress in 1960, in order to provide an infrastructure and resources to those investigators conducting primate research. There are currently eight NPRCs: California, New England, Oregon, Southwest, Tulane, Washington, Wisconsin and Yerkes. Supported by the NIH, these centres have more than 20,000 individuals of 20 different primate species. Seven of the eight were awarded over $57 million in fiscal year 1999 (7), before the Southwest Foundation for Biomedical Research joined the NPRC system. Additional government funded primate resources include the Caribbean Primate Research Center, a squirrel monkey colony at the University of South Alabama, a baboon research resource at the University of Oklahoma, and chimpanzee centres at the University of Texas (at the M.D. Anderson Cancer Center), and the University of Louisiana (at the Lafayette New Iberia Research Center). Other resources in the USA include private breeding facilities, some of which receive some federal funding.

The NIH recently conducted a survey pertaining to the NPRCs in order to "learn about investigator access to non-human primate resources" and to "assess current and future non-human primate needs" (7). A total of 641 investigators who received government funding in 1999 for primate research were surveyed. Those surveyed used a total of 13,000 non-human primates in research that year, and approximately 50% were rhesus macaques. The most common research areas cited were neuroscience, behaviour, physiology, immunology, infectious diseases, pathobiology, AIDS and virology. The main complaint of the investigators was that non-human primates are difficult to obtain. Therefore, two of the final recommendations made in the report were to increase breeding and increase funding/decrease costs.

Methods

The analysis conducted by The HSUS provides an overall picture of primate research in the USA. Two databases were utilised: Computer Retrieval of Information on Scientific Projects (CRISP) and PubMed. PubMed is a National Library of Medicine database that contains 11 million citations from over 4500 journals. CRISP, the primary source of data consulted, is a database of federally funded extramural biomedical research projects. Consequently, our CRISP analysis does not include information about research conducted by private research institutions nor intramural research conducted within NIH.

We analysed non-human ape (hereafter referred to as ape) and monkey research separately; consequently, the findings are presented separately. The analysis did not address the use of prosimians in research.

Ape research

A total of 184 grant abstracts in CRISP (awarded between January 2000 and May 2002) and 89 journal articles cited in PubMed (published between January 2000 and June 2002) were analysed with regard to ape research. These were all of the grants and publications pertaining to laboratory research on chimpanzees for those time periods in those databases. In order to analyse information for a time span of two full calendar years, we gathered information for all of 2000 and 2001. However, we also wanted to analyse the most recent information available; therefore, we examined information up to and including the month during which the analyses were conducted in 2002.

In attempting to determine the level of invasiveness of the research, the following practices were classified as invasive: inoculation with an infectious agent, surgery or biopsy conducted for the sake of research and not for the sake of the non-human primate, and/or drug testing. "Minimally invasive" indicates that a minor procedure, such as venipuncture, was performed. Finally, "non-invasive" indicates that the animal received no physical or psychological insult.

In order to determine funding provided for each project, we used the website of the Office of Extramural Research at NIH (8). This website lists all grants awarded per year, per state.

Monkey research

A total of 953 grant abstracts involving monkey research for January 2000–July 2002 were analysed — this represents approximately 20% of the total number of monkey research grants during this time period. As with the chimpanzee analysis, we wanted an analysis of a complete time span of two calendar years and also wanted to include the most recent information available. Initially, the first 1000 grants (listed in CRISP when specific keywords were searched) were to be analysed, but some were excluded, due to search results that did not actually involve monkey research (for example, an abstract may have referred to previous research using monkeys, but did not currently involve use of monkeys). As mentioned above, this analysis included monkeys only, and therefore excluded prosimians.

A PubMed analysis has not yet been conducted due to the enormous number of grants and publications to analyse; however, this sampling of extramural research grants is representative of federally funded monkey research overall.

The same definitions of invasiveness used for the chimpanzee (methods section above) were also used for the monkey research analysis. Also, the NIH extramural awards site was used to determine funding for each project, as was done for the chimpanzee research (8).

Results

Apes

In the USA, the chimpanzee (*Pan troglodytes*) is the only ape species used in biomedical research, and this was confirmed by our analysis. The databases consulted did not enable us to determine exactly how many chimpanzees were used in research during the reviewed time frame.

Information regarding how chimpanzees are housed in laboratories (individual vs. social) is limited. The CRISP analysis did not provide enough information to make an estimate. According to the PubMed analysis, 24% of the articles indicated that the animals were group housed, 25% indicated that they followed the *Guide for the Care and Use of Laboratory Animals* (which does not give a clarification either way), and 50% did not mention housing at all.

We examined fields of research, both biomedical and otherwise (i.e. behaviour of the species), in order to determine the types of research for which chimpanzees are utilised. Both analyses indicate that hepatitis (various strains) is the field of biomedical research for which chimpanzees are most commonly used. Other common research areas (biomedical and otherwise) include HIV, behaviour, reproduction (as a model for human reproduction), genetics, malaria, respiratory viruses, infectious disease and drug testing (Figures 1 and 2).

The funding analysis revealed that approximately $25–30 million per year of federal funding was distributed to 26 institutions for chimpanzee research and daily care (Figure 3). Therefore, this funding includes money designated for the daily care of the animals, as well as the money related to the research being conducted.

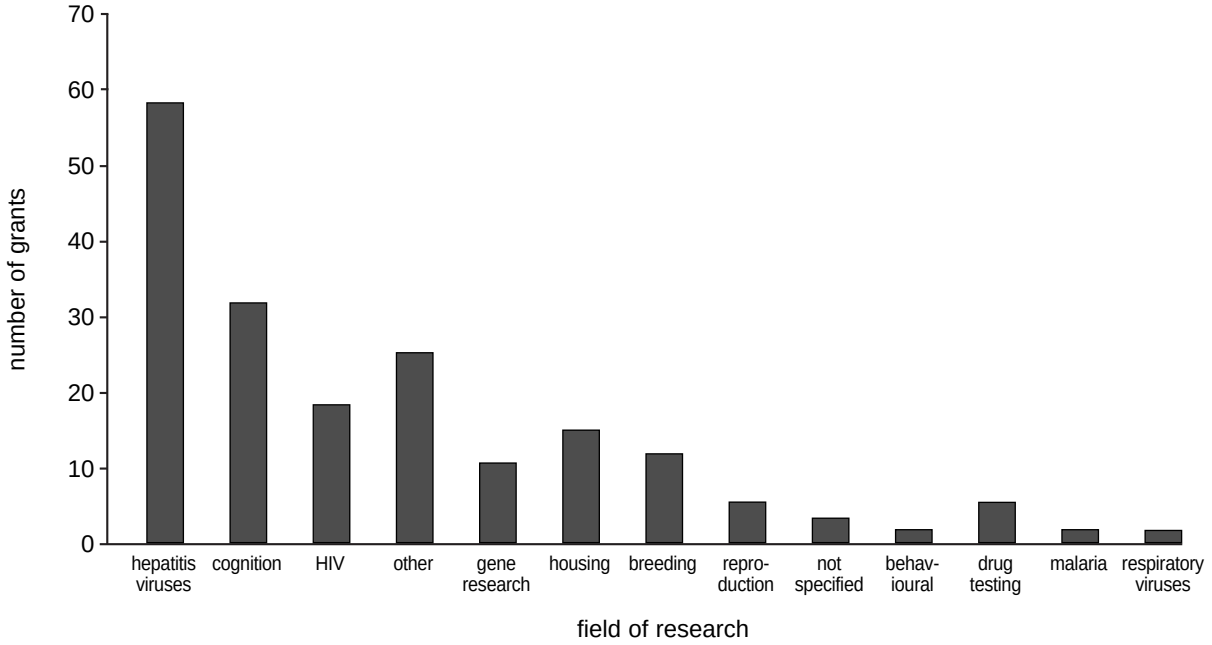
Based on the definitions of invasive (above), the CRISP analysis revealed that 23% of the grants were non-invasive, 9% were minimally invasive, 59% were invasive procedures, and 9% could not be categorised from the information provided.

Monkeys

The number of monkeys used in research could not be determined from the information provided in the CRISP abstracts, as was the case with chimpanzee research. With regard to the type of housing, 89% of the grants did not specify type of housing.

Approximately 27% of the funding dedicated to monkey research pertained to the study of HIV, followed by colony management (this number is expected to be high due to the high costs of housing non-human primates), neurological, reproductive (as a model for human reproduction) and behavioural research. Monkeys were also used for drug

Figure 1: Fields of research for which chimpanzees are utilised (data from CRISP analysis)



testing, ageing, cognition, infectious disease research and other studies (Figure 4).

Approximately $160 million per year was devoted to the monkey-related grant projects analysed, which represents only 20% of the total number of grants (Figure 5). In order to estimate funding for 100% of the monkey research, there were several factors to consider. For example, the NIH awards individual project grants, as well as base grants, which are large grants that are distributed by the institution for different projects (we will call these subprojects). Therefore, if the $160 million per year (individual grants and base grants) is multiplied by five in order to estimate total funding, the figure

Figure 2: Fields of research for which chimpanzees are utilised (data from PubMed analysis)

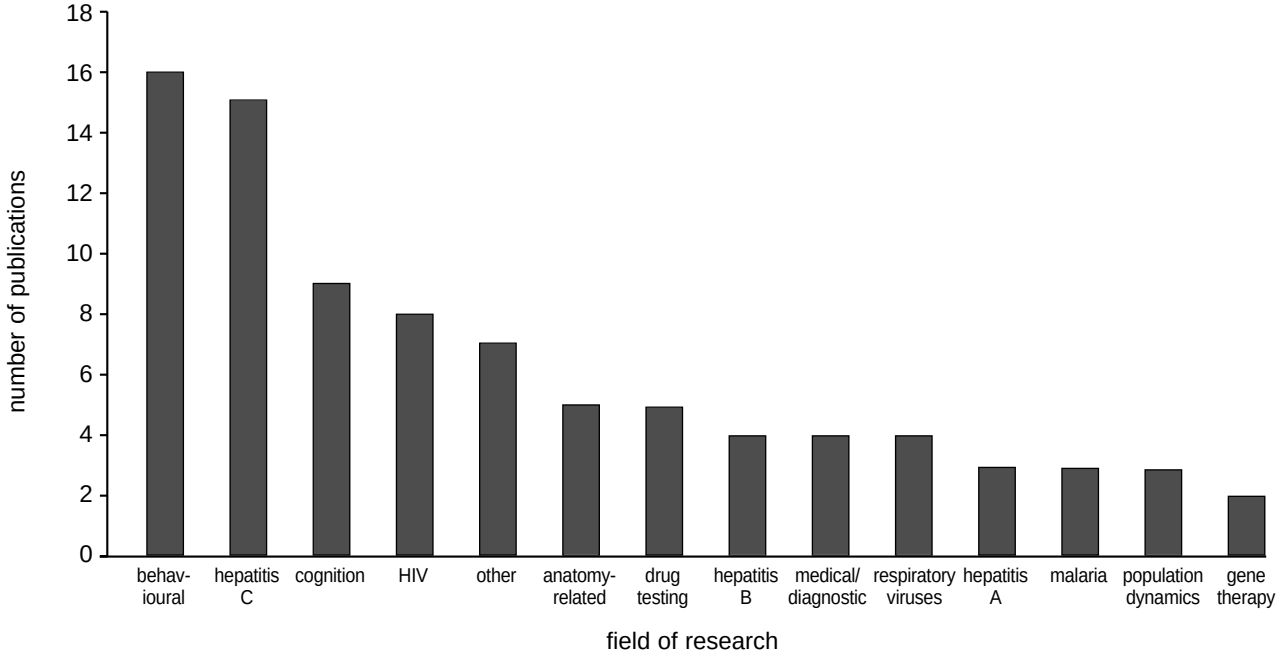
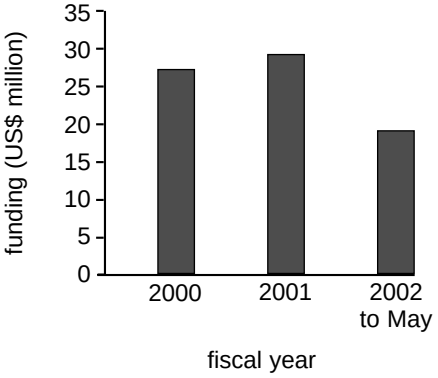


Figure 3: Government funding for chimpanzee research



would be $800 million. However, this may be an overestimation; the nature of the CRISP search has probably allowed more than 20% of the base grants to be included in the analysis, as there are many subprojects listed for each base grant. Moreover, some of the funding from each base grant is probably distributed to non-primate research. Taking this into consideration, we considered that a better estimation might be to multiply the base grants by two and the individual projects by five. If this were done, the total funding would be $575 million per year. In conclusion, we estimate that anywhere from $575–800 million is devoted annually to monkey research.

It was determined that 77% of the monkey grants involved invasive procedures; 12% were minimally invasive; 8% non-invasive; and 3% unknown.

Finally, the species analysis indicates that 45% of the total number of grants involved rhesus macaques, the most widely used non-human primate species in research. This finding is consistent with the survey conducted by the NIH discussed earlier (7). Baboons were used in 11% of the grants, followed by unspecified monkey and unspecified macaque. Other specified species reported were cynomolgus macaques, pig-tailed macaques, marmosets, squirrel monkeys and tamarins (Figure 6).

Discussion

The preceding analysis gives an overall current picture of primate research in the USA. Both chimpanzees and monkeys are used in a wide range of research areas, including various strains of hepatitis (the most common research for which chimpanzees are utilised), HIV (the most common

Figure 4: Funding for individual monkey research grants per field of research (based on 20% of the monkey research grants)

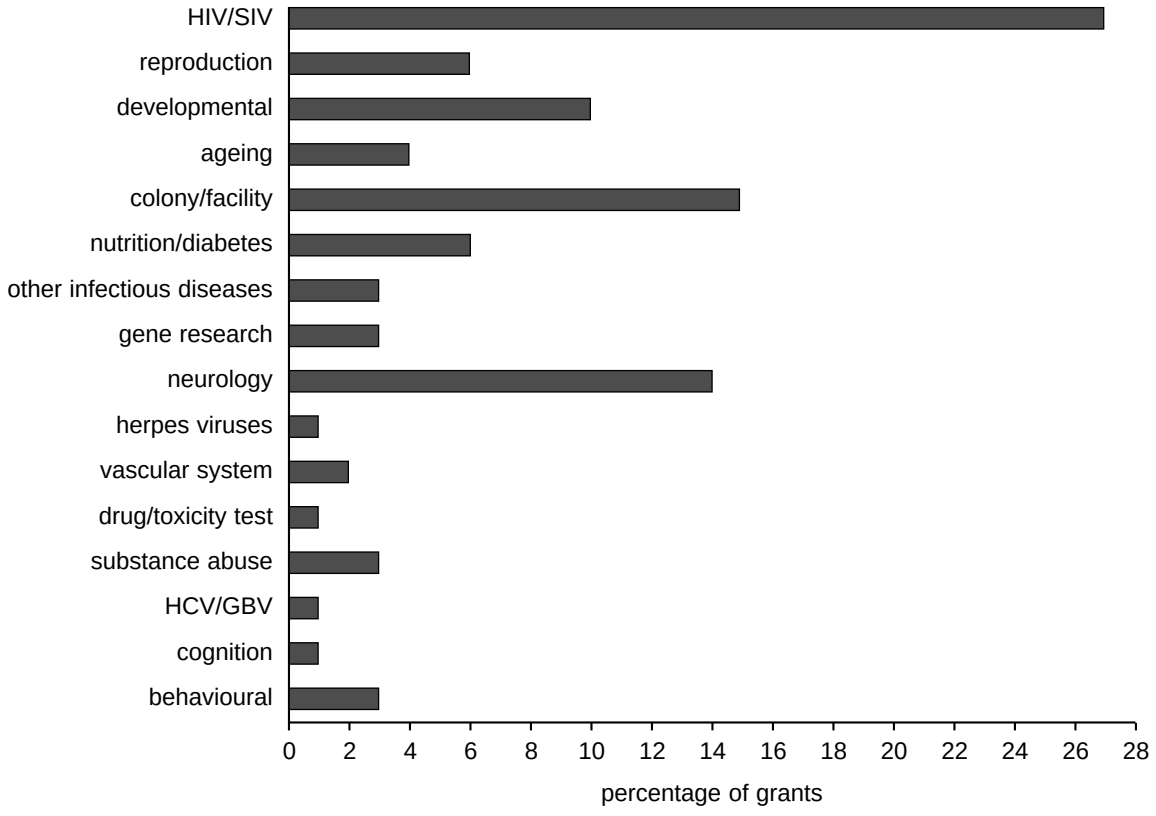
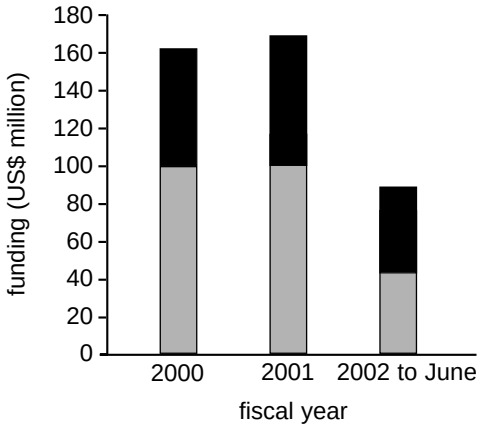


Figure 5: Government funding for 20% of the projects and subprojects involving monkey research



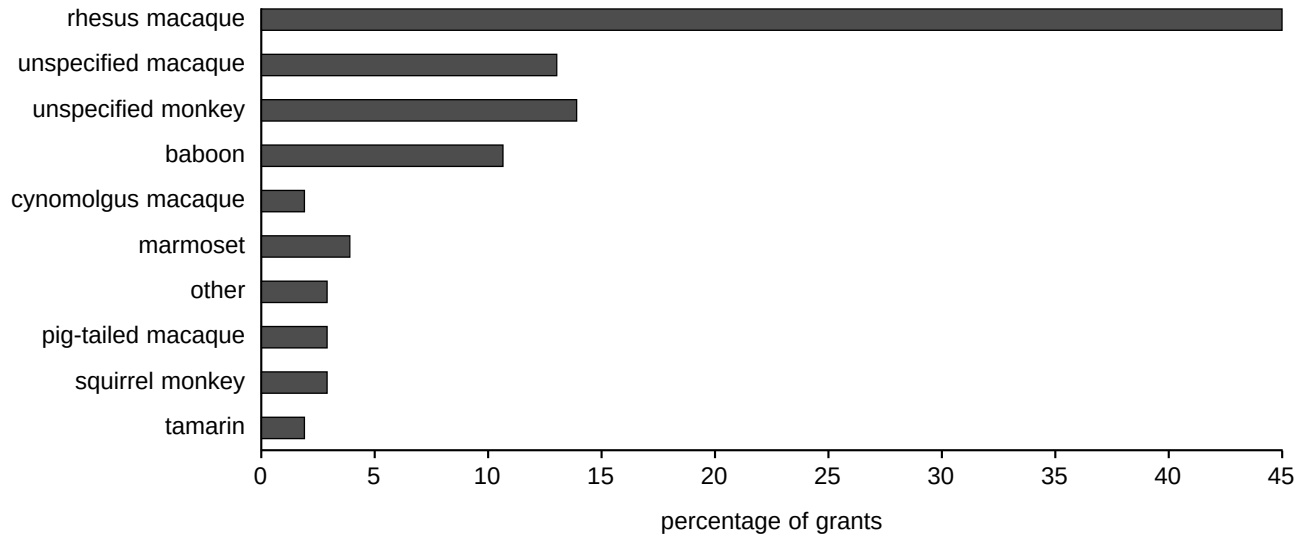
■ = *individual project funding;* □ = *subproject funding.*

research for which monkeys are utilised), neurology, behaviour, reproduction and malaria, as well as many other fields, with rhesus macaques being the most common monkey species used. It is estimated that the federal government spends approximately $25–30 million per year on chimpanzee research and $575–800 million per year on monkey research and care. We also found that the majority of chimpanzee and monkey research involves invasive procedures, at 59% and 77%, respectively. It became evident that there is significant information of importance missing from the CRISP abstracts, as well as the scientific publications, such as the number of animals used per study and the housing conditions in which the animals lived. The HSUS recommends that inclusion of this information should be required in the future.

Despite the fact that we were unable to determine the number of chimpanzees used in research in our analysis, a report from the NIH to Congress in 2001 indicated that, in 2001, approximately 1500–1600 chimpanzees at 13 institutions in the USA may have been used in federally supported research (9). A census conducted by the Great Ape Project confirms this number. With regard to the number of monkeys used for research, the only available information is provided in the USDA Annual Reports. According to the USDA Animal Welfare Report for Fiscal Year 2000 (the most recent available), a total of 57,518 non-human primates were used in research in 2000 (10). However, this number includes monkeys, apes and prosimians and only reflects the number of animals actually used in research; animals used for breeding purposes or those simply being held are not included. The total number may also be larger than that reported by the USDA, due to the fact that 22 institutions did not submit a report in a timely fashion, and therefore, were not included in the tabulation.

Also, despite the fact that housing conditions could not be determined, according to the Animal & Plant Health Inspection Service (APHIS) *Animal Care Report* of Winter 2001, "65% of primates in research are pair/group housed, with only 13% having no contact with other primates". However, few details of this survey are publicly available. If the survey included all non-human primates in laboratories, this number may be misleading. As previously mentioned, the total number of non-human

Figure 6: Species of monkeys used in federally funded biomedical research and testing by percentage of grants (based on 20% of monkey research grants)



primates reported by USDA includes only those which were used in active research protocols. Therefore, if this survey included breeders, it cannot be determined how the non-human primates used in research protocols were housed. It is likely that the majority of those used in research are individually housed. Furthermore, the definitions of pair-housing and no contact were not specified (some institutions may count monkeys who are able to touch each other through a mesh as pair-housed), adding more confusion as to exactly what the results of the survey mean.

One thing that is clear is that the USA uses more primates in research than any other country in the world — more than five times the number used in the entire European Union (approximately 58,000 vs. 11,000). Given this heavy usage, we believe the US government has an obligation to take a very close look at all of the available information (both present and historical) and conduct a cost–benefit analysis of primate research in order to assess "value added" to relevant fields of research and whether the use of primates is the only, or most effective, strategy for biomedical progress. The government should also immediately increase funding for primate-related Three Rs efforts in order to reduce, and eventually eliminate, the primate use in research in the USA.

If we look beyond the present analysis, what does the future hold? Recent events and publications indicate that the use of non-human primates in research is expected to rise, particularly in the near future. For example, various institutions have expanded their primate facilities, including the Oregon and California National Primate Research Centers and the New Iberia Research Center (11). A privately owned breeding colony, which is expected to house approximately 3000 non-human primates, is being established in Florida. Also, the NIH published a request for application on February 28, 2002, regarding the establishment of additional specific pathogen-free (SPF) primate breeding colonies.

The Institute for Laboratory Animal Research of the National Academy of Sciences held a workshop entitled *International Perspectives: The Future of Non-human Primate Resources* in April 2002. The research community discussed the increased need for non-human primates for research and the various primate resources throughout the world. In October 2002, the Association of Primate Veterinarians, the Office of Laboratory Animal Welfare and American Society of Laboratory Animal Practitioners held a workshop entitled *Emerging Uses of Non-human Primates in Biomedical Research* at which the research community discussed innovative uses of non-human primates and the potential challenges to Institutional Animal Care and Use Committees in addressing such research. Finally, the European Commission published a document entitled *The Need for Non-human Primates in Biomedical Research* in 2002. These recent events and actions clearly foreshadow a future increase in non-human primate research.

It is now time for the USA to follow other nations in ending research on chimpanzees. Therefore, The HSUS is calling for the use of apes in biomedical research and testing in the USA to be phased out expeditiously. The physiological and behavioural similarities between humans and apes are often used as justification for conducting biomedical research on apes, yet these are the very reasons why their use poses serious ethical concerns. For example, chimpanzees have complex mental abilities, including self-conception, anticipation of future events, mathematical skills, tool use and so on. Despite these similarities, there are enough biological differences between humans and apes that extrapolation of chimpanzee research results to humans is problematic; thus, a ban would highly benefit the chimpanzees and would not have negative effects on biomedical progress. One of the Boyd Group papers (6) discusses in depth the various mental abilities of apes and concludes:

These abilities are likely to enhance the Great Apes' capacities for suffering to such an extent that it is unethical to confine them in laboratory housing and use them in scientific procedures. A ban on the use of Great Apes in research and testing (as currently in place in the UK) is strongly supported on these grounds, as well as on grounds of conservation of species in the wild, and should be respected worldwide.

In summary, we hope this preliminary analysis of primate research in the USA proves useful in focusing attention on the alleviation of pain and distress in non-human primate research, the reduction and ultimate elimination of the use of non-human primates in research altogether, with priority given to phasing out the use of apes from research.

Conclusions

1. Non-human primates are used extensively in research in the USA, the majority of which is invasive. This scale of use clearly prompts the need for a cost–benefit analysis of non-human primate research in order to determine whether non-human primates are the only, or most effective, strategy for biomedical progress.

2. There has been a shift to ending the use of chimpanzees in research throughout the world. It is now time to ban the use of apes in research in the USA and worldwide.

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