Same same but different – a look at primates in Research

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It doesn't take a science degree or a chromosomal profile to be able to see that nonhuman primates (NHP) are a lot like us. It's their sameness to humans that makes them so popular for scientific study. But researchers say that animals are different to us and that is why it's okay to experiment on them. This is obviously a paradox.

In the book 'Next of Kin, My Conversations with Chimpanzees', Roger Fouts tells of his life long relationship with chimpanzees. He talks of their empathy and their ability to communicate via sign language and claims that they are part of the 'moral community' of humans. He said that to justify biomedical research on these animals because we deny our kinship with them 'draws a parallel from gruesome experiments on Jews during World War II and on mentally retarded people…to the extensive research on chimpanzees…' (2000)

So where is that fine line that separates atrocities from the pursuit of knowledge, and is the well being of the human race the only consideration? And it must be remembered that it's only a portion of the human race that benefits from state of the art medical research; developing nations are not so well off. During the Nuremburg trials it was said that research without informed consent is abhorrent and cannot be condoned. That apparently only applied to the human species. Although these highly philosophical questions are vital to any discussion of the use of NHPs in research, the practicality of the matter is that primates *are* used. They undergo removal from their families, imprisonment, unrelieved pain and finally they are killed so that human members of the developed world can live longer. The long term goal is to ban their use altogether, and even the researchers themselves admit that there is room for improvement. But in the meantime what can we, as a society, do to improve their conditions and reduce the number used?

There is a cloak of secrecy surrounding research involving NHPs. Numbers of animals used and the types of experiments or the amount of suffering endured is not readily available to the public. Many researchers claim that it is because of the blatant hostility that they endure from anti-vivisectionists, that they are forced to work in secrecy. Animal rights activists claim that if the work was worthwhile and humane, then researchers would bring it out in the open for everyone to see.

To help people get a picture of the use of NHPs in research I will give an overview of the situation. Then I will discuss some of the issues.

The single order of Primates consists of man and around 200 other species. NHPs are found in Africa, South East Asia and South and Central America. They have complex social organisations, with bonds based on attachment, friendship and kinship. They have the ability to learn, compete, cooperate, and prevent conflict.

The super family of primates known as the great apes consists of bonobos, gorillas, chimpanzees, orangutans and man, these animals are the most closely related to man on a genetic level.

The numbers:

Although the use of animals in research is decreasing worldwide, primate use is on the rise. It is estimated that 100,000 primates are used each year, mostly in the United States of America, Europe and Japan. These numbers are estimates only because many countries do not have a register of how many NHPs are used in research or what studies they are used for. Australia is one of those.

The US is the world's largest user of primates for research, and data obtained from laboratory reports submitted to the US Department of Agriculture shows that use of NHPs has climbed from 57,518 in 2000 to 71,317 in 2010. But when primates used for breeding or otherwise held in laboratories, and those killed for tissue for invitro studies are included in the totals, it rises to 125,752. In 2010, 30,808 NHPs were in experiments involving pain and distress. And 1395 were in experiments involving unalleviated pain and distress. The main users are universities and private companies (AAVS, 2011).

In Australia 710 NHPs were used in 2009 for research, although figures from Western Australia, Northern Territory and Queensland were not available. Australia has three government funded primate breeding facilities, where marmosets, macaques and baboons are bred for supplying laboratories. In spite of this ready supply, Australia also imports pigtail and crab eating macaques from Indonesia (HRA, 2011).
The Great Apes family has been singled out as being the closest relative to man and therefore capable of suffering equally as much as humans. Their use in research is being phased out and they can only be used in the European Union and Australia under extreme conditions or for research that will benefit the survival of their own species.

In the US chimpanzees are the only great apes currently being used, and a working group of the National Institutes of Health is determining the future use of these primates and their subsequent retirement. The US and Gabon are the only countries still using great apes for research. The expense of keeping them is creating pressure and either through legislation or budgetary restriction their presence in the laboratory may be coming to an end. If both the US

and Gabon end this type of research it will be the first global moratorium against research for any non human species. (To keep updated go to website@navs.org)

If The Great Ape Protection Act is approved, the US government will ensure permanent retirement of approximately 1200 federally owned chimpanzees, some of whom have been in a laboratory for forty years.

Where do they come from?

Asian countries are the largest exporters of NHPs, although India banned primate exports in 1978 and Bangladesh a year later. China is the top exporter to the US and has at least forty breeding facilities and they are exhausting natural populations of NHPs. Mauritius is the second largest exporter. www.aavs.org

There are four different methods of producing primate populations and these are:

Free range colonies, semi free range corral colonies, pen or run type single male harem colonies and colonies where animals are cage mated.

Although most countries have banned the use of wild caught primates it is known to be continuing.

Types of research

The main use for NHPs is pharmaceutical toxicology testing, research of infectious disease such as AIDS, malaria, tuberculosis, Ebola, cardio vascular disease, reproduction, drug abuse, xenotransplantation (organ transplant), vaccinations, bioterrorism, dentistry and neurosciences.

The estimated investment on research and development using NHPs in the EU reached 3500 million pounds in 2004 (Weatherall, 2006).

The issues:

There are shortcomings in the way NHPs are housed, cared for and transported and importantly the policy of minimizing the number of experiments on these highly intelligent animals is falling short as much of the research is not used.

Ethical issues or why strict guidelines for care are not effective

Transport Illness:

NHPs are transported over vast distances. Flights can be up to 3 days and involving several moves from their cage to small transport cages, transferring to airline crates and being trucked

to the airport, they may also have flight changes in transit. This is then all repeated at the destination, then after acclimatising to quarantine they are transferred to a laboratory. In the US in 2009 582 monkeys died in quarantine (AAVS 2011).

It can take as long as several months for the monkeys to return to their normal condition and this then has an effect on their function as a research tool.

Wild caught

Primates suffer a high level of stress when caught from the wild and sold to laboratories. They have a great potential for injury and psychological distress through fracturing of family groups, suboptimal housing during transport, long transport times often with many flight changes, and noise, temperature and pressure variations that leave them stressed and fearful. Whilst most countries have banned the use of wild caught primates the practice continues as shown by The British Union for the Abolition of Vivisection on their website. http://org/our-campaigns/primate-campaign/buav-primate-trade-investigation

The National Health and Medical Research Council (NHMRC) in Australia has stated that 'Non human primates …must not be taken from wild populations', but the BUAV report showed that this is a farce as the animals are taken from the wild, placed on Tinjil Island in identical conditions and then transported to Australia. When these animals are held prior to transport from Indonesia, the pens are cramped and barren with no shelter, fresh air or sunlight, limited water and food and dirty conditions. (http://www.youtube.com/watch?v=brKbWMmvWZo)

Thirty percent of NHPs imported to the US were caught in the wild or were bred from wild caught in 2010 (AAVS 2011).

Housing details

Uprooting NHPs from their social and family structures causes extreme distress for these animals, not only for those that are taken but also the ones left behind. NHPs are often housed, individually in the research facilities in small cages, with none of the environment or community that is vital to their species. Many animals will exhibit behavior that indicates their distress such as rocking, head-twisting, pacing and also more extreme behaviors such as self-biting, eye-poking, body throwing and head-banging.

B**ehind closed doors**

It is difficult to reconcile claims by research institutions that NHPs are treated humanely and that they endure only limited suffering, with some of the readily available examples. A cursory glance of many research articles will indicate that 'humane' is a subjective term.

Here are a few examples:

Neurological studies on NHPs can include being strapped into a primate chair, deprived of water for up to 8 hours a day. They may have surgery performed on their brains with parts of it damaged and monitoring devices being implanted. In 2002 BUAV conducted an investigation in the primate brain research centre at University of Cambridge and collected evidence of monkeys being deliberately brain damaged (cutting or sucking out parts of the brain, injecting toxins), training and testing through water deprivation and food restriction, brain grafts, and gene therapy. Many died or had to be killed and for some, surgery needed to be postponed as the monkeys were not properly anaesthetized. Experiments could last for two years.

Covance is a multibillion dollar contract research facility and in Munster Germany BUAV found macaques being physically abused by some handlers. (http://www.buav.org/our-campaigns/primate-campaign/buav-primate 2003)

An example of neurological research conducted on NHPs is studies of stroke. Out of 912 treatments that were effective in animals, 114 were trialed on humans and all were found to be ineffective (Ménache 2010).

In another study infant monkeys were removed from their mothers and housed individually in a cage or with other infants in order to find out if mothers breed quicker when their infants are taken away from them early. It was discovered that young isolated monkeys became depressed and missed their mothers and the mothers actually bred at a slower rate (Reinhardt 2002).

An experiment using baboons involved researchers delivering mother baboons of their babies prematurely. The babies were then killed so that parts of their anatomy could be studied. Although a similar study had been conducted before from pathology samples on human premature babies, and research had also been conducted on lambs in 2004, and not forgetting that glucocorticoids have been in use for premature labour since mid last century researchers felt they had more control of variables by using baboons (Gubhaju, Black, Sutherland, Yoder, Zulli and Bertram 2009).

Poor retrospective reports of animal suffering

In 2002 the European Commission responded to increasing criticism of primate trade and research by commissioning 'The Welfare of Non-human Primates used in Research'. It reported that current datasets concentrate on the number of animals used in experiments, but they do not cover the severity of the experimental procedures. Animal suffering is poorly recorded and is often only considered prospectively when the research is being presented to an ethics

committee. The authors suggest retrospective reporting by animal welfare agents and veterinarians including details on the severity of procedures for NHPs. They say that study journals should include details of animal suffering and be provided as the final reports are handed over by the scientists to the granting bodies.

Skill of handlers reduces animal's stress

A United Kingdom report by the Universities Federation for Animal Welfare in 2006 found that more education was needed for handlers to train primates. This would help the primates to cooperate with activities such as blood sampling and administering of chemicals so that the situation would be less stressful. But they said there was a lack of enthusiasm due to cost, not wanting to change, and lack of communication. They state that 'inhumanity arising as a direct result of the use of animals in science should be reduced as far as possible'. They also said that lower stress levels of primates meant more reliable results from an experimental point of view, but this concept was slow to catch on.

No retirement plan for Aussie primates

The National Breeding Colonies in Australia will not generally accept animals that have been used for scientific purposes. In most cases, killing the animals is the only option when the study has been completed, as there are no retirement facilities for primates, even though other developed nations have them.

Rubber stamping by ethics committees and welfare groups

Ethics committees are in place as a way to ensure that research being conducted does not cross any ethical boundaries. Applications are made to the ethics committee before commencement of any research. The failing of these committees is that they are numerically dominated by members affiliated with the research department. Dr Denise Russell stated that they were a way of making the unpalatable look more acceptable and that there was no discussion of using non-animal alternatives. Members must sign a confidentiality agreement so that the public is uninformed about how many experiments are conducted, the number of animals used and the distress inflicted on them. The reality of ethics committees is that most research is not rejected.

An ethics committee always includes a category D person who is a community member and this covers the concept of liaising with the public. The confidentiality clause prevents this community person discussing research with the rest of the community and as they are also outvoted within the committee their function is limited. There is also difficulty for a lay person or a welfare representative to understand specialized, complex, scientific research, and it is even more difficult for them to offer a non-animal replacement (HRA 2009).

Animal welfare groups are in place to ensure the humane treatment of animals used in research, but their effectiveness depends again on the bias built into them. For example, the European report, 'The Welfare of Non-human Primates used in Research' is compiled by a large cross section of specialists with many animal welfare representatives. In contrast Australia's National Health and Medical Research Committee, provides its own welfare committee, which means that there is no outside input into animal welfare within Australia. Although there are groups overseeing animal research such as the NSW Animal Research Review Panel, the people on these panels are again controlled by confidentiality clauses.

The science of it all and why the research is not necessary for the health and well being of the human race

 # Stress affects results

Stanford neuroscientist Robert Sapolsky (2007) has shown that apes and monkeys are intelligent and social animals, and that they respond to stress in a similar way to humans by releasing adrenalin and glucocorticoids. Chronic levels of these hormones lead to conditions such as diabetes, gastrointestinal disorders and high blood pressure. With prolonged stress, brain function, particularly areas of learning, memory and judgment, is affected. He also showed that a good social structure was the best protection against stress related disease. André Ménache of Antidote Europe said that lack of predictability will flaw results because the animals are stressed and not in their natural environment (2010).

Results are distorted by unpleasant laboratory environments and procedures. These distortions affect the animals' susceptibility to and progression of disease, differing absorption, tissue distribution, metabolism and excretion of chemotherapeutic agents and differences in the toxicity and efficacy of pharmaceuticals.

 # Same same but different

It makes sense that although we are similar to chimpanzees, our closest relatives, there are also some striking differences, and these differences are present on a genetic level. Although we shared a common ancestor with chimpanzees five to seven million years ago, there is an estimated difference of four to five percent genetically speaking. Most of these genetic differences lie within the regulatory regions of our DNA and can exert a follow on effect upon hundreds of other genes. So a small difference has a big effect. We don't look the same and even a monkey brain is not a scaled down version of a human brain. There are differences in the cortex, the number of synapses and visual areas.

 # Research not used

Much of the research conducted becomes buried in a slush pile, never to be used in the pursuit of medical breakthroughs. Andrew Knight found that out of 95 experiments, almost half were not cited by any subsequent papers. Only 14.7% of all invasive chimp studies were cited by papers in relation to diagnostic methods for combating human disease. Further examination showed that other disciplines such as in-vitro studies, human clinical and epidemiological studies, molecular assays and genomic studies contributed most to their development. None of the chimpanzee studies demonstrated an essential contribution (2011).

Lack of coordination

Discussion between researchers, learned societies and other stakeholders about the changing research technologies and how they affect the need for ongoing NHP research creates a scenario of inefficiency. As new technology, such as imaging techniques, is developed there needs to be a systematic review between the major players in the research field; the research institutions, governments and animal welfare proponents, so that less NHPs are used.

Which way for the future?

The ultimate goal is that NHPs are not used in any research, but given that there is strong support for their continued use (particularly by financial stakeholders) there are short term improvements that would help reduce the number of animals used and to improve their conditions.

In 2006 a working group for the European Union consisting of six university-based researchers, one environmentalist, one animal behaviorist and a broadcaster produced, 'The use of nonhuman primates in research'. In it they proposed a series of recommendations as follows. Although many of them were reiterating their need to use NHPs in research (not surprising given the weighting of researchers), several were about improving conditions so that fewer animals were needed.

- Disseminating information gained from the research to funding bodies, ethics committees and regulating agencies.
- Systematic reviews by funding bodies
- Funding organisations to encourage and fund growth of alternatives to NHPs
- Retrospective reporting on the severity of procedures
- Journaling of the suffering endured by NHPs and steps taken to remedy the situation.
- Public registers for toxicology studies on NHPs
- Engagement of the public around issues of science and the use of animals

Further recommendations to be explored are:

- Retirement sanctuaries for NHPs who are no longer required for studies.
- National and international registers so that researchers can access previous research easily, thus reducing duplication
- Tissue databases readily available internationally and gained from humans

The use of animals in research creates sorrow in the hearts of all people who respect the sentience and uniqueness of non human animals, however, the use of NHPs has become an even more emotive issue, as we can see that these animals have complex brains, social systems and personal relationships. In short, they have the capacity to feel just like we do.

The use of NHPs in research subjects these sensitive creatures to an unnatural life in a laboratory, enduring pain purely so a privileged section of their closest relatives can enjoy the benefits of an advanced medical system. Regardless of whether there are alternatives available, their use in this manner is unethical and is part of a long history of dominant forces using the helpless to further their own benefits. But what makes this scenario even worse is that there *are* alternatives such as efficient preventative care, epidemiology, pathology, microdosing and state of the art imaging techniques, just to name a few. Major disease research facilities such as the Cancer Council are using tools such as population studies, pathology, imaging, clinical trials and tissue data bases as more accurate and efficient means of health discovery.

Perfect health is a western concept that is failing as individuals take less responsibility for their own health, for example problems of obesity, smoking, drinking and fast food. State of the art medical science benefits only a portion of the human race, and this is the portion with habits of overconsumption.

The human race has a long history of treacherous behavior in the name of science, with experiments conducted on Negros in the 1800s through to the study of the mentally retarded and dissection of their brains in Germany in the 1940s. Along with treacherous behavior there have always been the silent bystanders. Opening up the practice of conducting research on primates and engaging people in its discussion will make researchers and their funding bodies more accountable. Although researchers are the obvious target it's important to remember that there is a huge industry spanning from illegal poachers, breeding colonies, contract laboratories, drug companies and universities which back this research. These industries need to be made accountable and silence must be replaced by transparency and communication. The only way to achieve these changes is through rational discussion and knowledge.

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