

National Anti-Vivisection Society and Lord Dowding Fund for Humane Research

Monkeys & Men

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Jan Creamer / NAVS

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An assessment of the use of primates
and non-animal techniques
in neuroscience research

Evidence presented to the Cambridge Primate Centre Planning Inquiry

Introduction

Public Inquiry Held into an Appeal by the Chancellor, Masters and Scholars of Cambridge University against the decision of South Cambridgeshire District Council

Appeal Ref: APP/W0530/A/02/1090108

Site at 307 Huntingdon Road, Girton, Cambridge

Submission to the Public Inquiry 26 November 2002: Evidence of the National Anti-Vivisection Society and Lord Dowding Fund for Humane Research Against the University's assertion that an animal laboratory is in the public interest.

1. The National Anti-Vivisection Society (NAVS) was founded in 1875 and is the world's longest-established group of its kind; the NAVS has enjoyed widespread political and high profile support since its inception, from Lord Shaftesbury and Queen Victoria in our early days, to leading politicians, key figures, and scientists today.
2. The Lord Dowding Fund (LDF) is a department of the NAVS which provides grants to scientists conducting scientific and medical research without the use of animals. The Fund's annual research budget is similar to that spent on alternative research projects by the Home Office's Animal Procedures Committee – in the region of £250,000 per annum.
3. In this submission to the public inquiry, the NAVS and LDF will argue against permission for the building of a new primate facility at Cambridge University, and present our evidence in three sections:

Section 1: National interest

4. We will discuss the assertion that the proposed primate laboratory is 'nationally important', and contrast this with non-animal neurological research already being carried out in the UK. We will explore the potential for creating a centre of excellence which does not involve the use of animals. We will present references to knowledge in the field of the central nervous system gained from studying people, and contrast this with research on primates. This will include the difficulties already encountered with the use of primates to replicate human disease, including differences in physiology, response to drugs, response to pain, and the difficulties when dealing with the human "feeling state".

Section 2: Differences between non-human primates and humans

5. Summary of evidence and discussion of known species differences, with particular reference to brain research; this relates to discussion in first section.

Section 3: Does a primate centre have a long-term future?

6. We will concentrate upon the external factors that are likely to prevent a primate centre from having a long-term, viable future. We will show that establishing a primate centre already goes against a trend of declining use of primates in nervous system studies. We discuss how

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this line of research is not only under pressure from developments in non-invasive human study, non-animal research generally, but also increased use of genetically modified animals (which will, for the foreseeable future, be rodents). We will argue that primate research is the most likely area of animal research to face national or international restriction in the coming decade, for the reasons stated above, and due to public concern about the use of primates, as well as public safety and animal welfare. We will also examine the impact of restrictions on duration of supply journeys, use of wild caught animals, and licences to experiment on non-human primates.



Section 1: National interest / 'national importance'

7. The NAVS and LDF address here, Cambridge University's assertion that the proposed primate laboratory is of national importance. It would appear that a key reason for a further appeal against refusal of planning permission is the importance attached to this facility, in terms of national science strategy.
8. It has been claimed that the primate laboratory would: (a) provide “*world class neuroscience*”, (b) “*consolidate the UK’s position as a global leader*”, and (c) bring together scientists to work in an inter-disciplinary environment using state-of-the-art facilities.
9. The objectives of the Government in wishing to see the UK lead the world in scientific effort is laudable, and something which everyone can support. After all, we all have a stake in good medical research. The issue here is whether a primate laboratory is in the national interest, and we would argue that it is not.
10. Many scientists are turning away from animal research, and most research is now carried out without the use of animals. The NAVS, and many others, do not believe that animal work is “world-class” or “leading edge”. Certainly, major developments in sophisticated non-animal techniques support our view that world-class science is in the field of non-animal research, with the focus on the study of human disease in human beings.
11. Ground-breaking, innovative neurological research is being conducted in the UK without the use of animals, such as at the Neurosciences Research Institute at Aston University.
12. Experience has shown that both behavioural neuroscience and other neurological experiments on animals are fundamentally flawed due to species differences (see later).

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Aston University: world class research,
based on study of humans:

13. Outside of Cambridge University, scientists are committed to promoting the UK as a centre of excellence without the use of animals. The Neurosciences Research Institute at Aston University is a prime example of such foresight, with its plans for a new 'Academy of Life Sciences' to open in April 2004. The £8 million Academy will provide the opportunity for innovative cross-disciplinary work by the integration of clinically related research in neuroscience. It will include research groups working on behavioural and cognitive sciences, neuroimaging, vision, ophthalmic and physiology optics.

The claims of the animal researchers who want the Cambridge centre:

14. Lord Sainsbury, minister at the Department of Trade and Industry, has written in support of the creation of a centre of excellence in neuroscience at Cambridge. As we said earlier, the NAVS and LDF are supportive of good medical research, but the minister is ill-advised to follow the line that use of animals is the best way to achieve progress.

15. In his letter of support, Lord Sainsbury quotes researchers from the field of animal neuroscience, who claim that the centre: *“promises internationally competitive science”* and will *“very likely advance our knowledge significantly in the field of central nervous control of behaviour”*. It is also claimed by those in the industry that *“Medical research, pharmaceutical research, and our knowledge of the brain/ mind, all will benefit enormously from this initiative”*.

16. We submit that the facts do not bear out these claims:
 - (a) the new non-animal techniques now developed avoid the underlying problem of animal research – that of species differences*.
 - (b) knowledge in the field of central nervous system control of human behaviour is constantly increasing, due to rapidly advancing, innovative technology in the field of neurology research for the study of human volunteers (see below). (*NB: The phrase “species differences” describes the differences in reaction observed between species to the same chemical or surgical intervention. Moreover, in the case of artificially-induced disease in laboratory animal models, there are often fundamental differences between the course and effects of the disease in the laboratory animal, and humans. Crucial differences between disease in genetically modified animal models of disease, and human patients, have also been noted. The next section, on species differences, refers).

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Medical research:

17. The physiological (the functional reactions in the body) response of an animal to a painful or distressing stimulus varies not only between species but between individuals and is determined by the genetic makeup of an animal¹.
 18. Non-human primates, despite their evolutionary closeness to us, are distinct from us in the way they express genes in the brain ('expression' of a gene is the activity or product that the gene causes to occur in the body). There are even big differences in gene expression between humans and chimps, although gene expression between chimps and other non-human primates is similar².
 19. Another hurdle when using animals to model human nerve diseases (or any other disease for that matter) that has not been overcome is that the human form of the disease can never be completely replicated in an animal. Animal models of the neurodegenerative disease Alzheimer's, for example, do not develop the characteristic 'neurofibrillary tangles' or show significant nervous system degeneration³.
- Pharmaceutical research:
20. One of the major causes of death in the western world is from adverse reactions to drugs despite that all pharmaceuticals have been tested on animals for safety and efficacy before entering the market.
 21. An anti-Parkinson's disease drug, tolcapone (Tasmar) was withdrawn from the market in 1998 for being linked to deaths from liver disease⁴. Similarly, the antidepressant Seroxat was also linked to liver damage, in 1997⁵. The safety of donepezil for Alzheimer's came under review in 1999 resulting in updating of product information⁶, and clinical trials of a potential Alzheimer's vaccine were suspended this year when participating patients began experiencing side-effects to the nervous system^{7,8}. The vaccine had been hailed as "*revolutionary ..following encouraging tests on animals*"⁹.
 22. Drugs which may appear to cure a disease which has been artificially induced in laboratory animals are not guaranteed to do the same for people. Only in humans can the relationship of subjective and discriminative drug effects be assessed at the same time¹⁰. The therapeutic effects of the appetite suppressant fenfluramine for autism and its potential to reduce suicidal tendencies, for example, were discovered in people and could not have been predicted in animal experiments¹¹.



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Knowledge of the brain/mind:

23. Little, if anything, can be gained by studying the brains/minds of non-human animals. The behavioural response of an animal to a painful or distressing stimulus varies not only between species but between individuals¹.
24. The processes involved in behavioural responses in humans are known to be more complex than in other species¹², and no animal species reacts to behaviour altering drugs in the same way as a human being would¹³. For example caffeine, which can induce panic attacks in people, has conflicting results in animal models of anxiety¹⁴.
25. As for the human “feeling state”, there is no parallel that can be drawn from animals, as they cannot tell us how they feel. Depression, for example, is a complex human reaction¹⁵ and there is no animal that can model the symptoms of schizophrenia¹⁶.

Primate Neuro-Research

26. Currently Cambridge neuroscientists are working on common marmosets. However, at the new £24 million centre for neuroscience proposed by the University of Cambridge they would conduct research on macaques as they believe marmosets do not make good models due to their small brains¹⁷.

Macaques as experimental models for human diseases:

27. An investigation by the NAVS at the Institute of Neurology in London found that in the Sobell Department of Neurophysiology, a researcher was using macaques for a study of the nerve connections between the brain and muscles of the hand. For the purpose of the experiments, the macaque skull was fitted with a headpiece and recording/stimulating electrodes in various parts of the brain. The intention was to study the effects of brain stimulation on learned tasks and to this effect wires were connected from the headpiece directly to selected muscles of the forelimbs. A dye was injected into the parts of the brain studied so that the nerve connections can be traced after the monkeys have been killed¹⁸.
28. However, it is unlikely that progress will be made in the study of the human brain by using laboratory animals. As researchers at two prestigious institutions, the Salk Institute and the University of California wrote: “*What is known about the neuroanatomy of the human brain? Do we have a human cortical map corresponding to that for the macaque? And what does the human equivalent of the connectional map look like? The shameful answer is that we do not have such detailed maps because, for obvious reasons, most of the experimental methods used on the macaque brain cannot be used on humans ...For other cortical regions, such as the language areas, we cannot use the macaque brain even as a rough guide as it probably lacks comparable regions*”^{18,19}.

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29. We submit that researchers need to concentrate on humans rather than monkeys; scanning techniques can be used to study human patients and volunteers, and human post mortem specimens can be studied, rather than studying brain function in macaques.



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Parkinson's disease research:

30. Parkinson's disease is unique to humans²⁰, slowly progressing, whereas in the artificial lab disease "model", using the drug MPTP, the disease is rapid in its course. There are differences in nerve degeneration and the transmission of nerve impulses in naturally-occurring human Parkinson's disease and MPTP-induced Parkinson's disease in animals²¹. Also, there are major differences at both the behavioural and neurochemical (nerve chemistry) levels between marmosets and cynomolgus monkeys when administered MPTP, making it impossible to predict with any certainty how results of macaque and marmoset experiments can be applicable to humans²².

Macaques:

31. One British researcher had been working on macaques to investigate treatment for Parkinson's disease since 1997. He had been inducing neurodegenerative symptoms of the disease in the macaques by giving them the MPTP and then performing surgery on the animals as an approach to "treatment".
32. However, the Home Office recently stopped this work, demanding further justification for the research and imposing modifications to experimental procedures¹⁷. In 1999 the government advisory body, the Animal Procedures Committee (APC), voiced concerns about the use of macaques in MPTP-induced Parkinson's disease. One reason was due to the differences in brain architecture between human beings and macaques, raising doubts about the transferability of results. Nevertheless, the APC decided to grant a project licence anyway²³.

Marmosets:

33. There are differences between MPTP-induced Parkinson's in marmosets and human Parkinson's patients – the absence of Lewy bodies (as seen in Parkinson's patients) in marmosets²³.
34. Previously, the rather poor reason given by researchers for the use of marmosets was their small size. Now, they are citing the difficulty as being that the animals' brains are too small¹⁷. Despite these drawbacks, an application relating to Parkinson's disease involving several hundred marmosets was seen and approved by the Animal Procedures Committee during 1999. The planned procedures were rated in the 'substantial' severity category²³.

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Parkinson's disease experiments on animals: non-animal replacement techniques:

35. In primate experiments where electrical activity of the brain is recorded after injection of drugs that affect brain function (MPTP), human patients could be studied instead with scanning techniques. Patients in whom Parkinson's disease has been induced with MPTP underwent brain scans using high resolution PET and the drug fluorodopa²⁴.
36. Surgical lesions in the brain, located by electrodes while the patient is still conscious, are a normal, common procedure in the treatment of Parkinson's and are known to be effective²⁵. A potentially successful new treatment method involves deep brain electrical stimulation^{26,27}.
37. Behavioural changes in patients in whom corrective lesions for Parkinson's disease have been made have been studied post-surgery by MRI scans of their brains²⁸.
38. Microelectrodes have been used in human patients for detection of the areas where lesions need to be made in the brain, for recording and stimulating. In this way, tremor and movement cells can be located²⁹.
39. The effect of patient's movement on the lesioned brain has been assessed in human Parkinsonian patients³⁰.

Other primate neurology research:

40. The following experiments carried out at three different institutions provide further evidence of the futility of neurological research using primates.

University of Cambridge:

41. The level of dopamine, a chemical found in the brain, was studied in the marmoset after destruction of an area of the brain with toxic chemicals, in order to assess the relationship of dopamine to disorders such as schizophrenia. Behaviour was studied as well as brain chemistry. When the monkeys had learned to retrieve objects, they were injected with amphetamines to see how this affected their performance. The study merely confirmed previous findings and furthermore, the researchers already knew that this type of brain damage affected behaviour³¹.

Oxford University:

42. An area of the brain was removed from macaque monkeys so that their performance of visual memory tasks could be compared with monkeys that had previously had a different part of the brain removed, and with normal monkeys³². It would have been more logical to study amnesic, brain-damaged patients rather than deliberately brain-damaged monkeys.

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43. In another experiment 32 lesions were made in the brains of six macaques so that the researchers could compare how monkeys with multiple lesions in their brains performed tasks, compared to those without lesions. In a pilot study, one monkey's brain was so badly damaged he could hardly move his arm but was still made to perform in 2000 trials of task training. The results contradicted those obtained from human studies³³.



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London:

44. At the Institute of Neurology electric shocks were given to the spinal nerves of 4 squirrel monkeys in order to compare nerve control of their arm movements with that of cats and macaque monkeys. The skull was opened and part of the spinal cord was deliberately damaged³⁴. The animals were fully anaesthetised during surgery, but the drug used for the remainder induces only light anaesthesia, has poor pain-relieving properties and is not recommended for non-human primates^{35,36}. The team had carried out this experiment on squirrel monkeys before, and the transmission of nerve impulses from this area of the brain and spinal cord has been studied by others, in people. The researchers stated: "*We recognise the dangers of making these comparisons both between laboratories and between species*".

Non-animal research in neurology:

45. An editorial comment from a scientific journal in the early 1990s provides an appropriate introduction: "*Until the early 1970s, knowledge about the living human brain had been derived mainly from surgical case studies. These were supplemented with behavioural observations of lab animals, many of whose brains had been physically altered through surgery. Today, sophisticated imaging techniques have opened more efficient, revealing - and certainly less bloody - avenues for neuroscience researchers. These techniques, formerly recognised primarily for their utility in diagnostic procedures, allow brain scientists to peek inside the skull non-invasively and with minimal trauma to the subject*"³⁷.

Humane Alternatives: Non-animal techniques better for humans and animals

46. Substantial evidence in the scientific and medical literature demonstrates that neurology research can progress without the use of animals.

Human brain imaging:

47. In recent decades a wealth of brain imaging techniques have been developed to assist neurologists with the non-invasive study of human brains. These include:
- Functional magnetic resonance imaging (fMRI) tracks brain activity by monitoring blood flow. This has allowed neuroscientists to understand which areas of the brain are active during specific tasks³⁸.

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- Positron Emission Tomography (PET) allows areas of the brain which are active during a specific task, such as thinking or experiencing pain, to be identified^{39,40}.
- Cortical Evoked Potentials (CEP) measures the electrical component of electromagnetic brain pulses and Magnetoencephalography (MEG) measures the magnetic component. In combination, CEP and MEG accurately identify areas of the brain involved in processing information for a specific activity³⁹.
- Transcranial magnetic stimulation (TMS) applies magnetic pulses to the brain which then stimulate or suppress activity. This has been used to study visual attention, memory and recognition³⁸.
- Repetitive TMS (rTMS) creates a virtual lesion for neuroscientists to experiment on just as they would by cutting the nerves in an animal's brain to see the functional response. Thought processes have been investigated using rTMS³⁸.
- A combination of TMS and fMRI is being used to probe changes occurring in the brain associated with diseases such as schizophrenia³⁸.
- A US study has used brain imaging techniques to investigate the brains of identical twins and fraternal pairs to understand how genetic factors influence the volume of grey brain matter. By knowing which parts of the brain are under genetic control researchers know where to look for brain degeneration in diseases such as schizophrenia⁴¹.
- Scientists supported by the Lord Dowding Fund have developed a new imaging technique known as Synthetic Aperture Magnetometry (SAM). By using measuring electrical and magnetic pulses SAM can identify the region of the brain responsible for signals and their depth when triggered by particular stimuli. SAM is currently being used to study the experience of pain associated with irritable bowel syndrome and non-cardiac chest pain⁴².

Molecular models:

48. Certain strains of *Escherichia coli* produce amyloid fibres similar to those that accumulate in the brains of Alzheimer's and other degenerative brain disorder patients. *E.coli* is therefore used as a molecular model to study amyloid formation during the design of drugs to treat or prevent human amyloid diseases⁴³.
49. Brain cells which need dopamine to function and those that do not can be isolated from human foetal brain tissue. Using this molecular model a study was performed to understand why the degeneration of dopamine dependent brain cells occurs in neurodegenerative disorders such as Parkinson's disease. A particular protein was identified as a causal factor in dopamine dependent brain cell death⁴⁴.

Patient studies:

50. The Lord Dowding Fund has supported research using Parkinson and schizophrenia patient volunteers to investigate visual abnormalities caused by the failure of dopamine systems in

Species Differences

the brain. The effectiveness of potential therapies are assessed by observing the effect on the patient's vision⁴⁵.



Epidemiological studies:

51. In the United States, nuns have donated their brains after death for research. This allows a unique insight into potential causes of Alzheimer's by studying the brains of people who have led similar lives so that many epidemiological variables are absent. It has already been discovered that the likelihood of someone contracting Alzheimer's can be predicted from linguistic abilities in their early twenties⁴⁶.

Alternative techniques, relevant to humans, are the future:

52. Outside of Cambridge University, scientists are committed to promoting the UK as a centre of excellence without the use of animals.
53. The Neurosciences Research Institute at Aston University is a prime example of such foresight, with its plans for a new 'Academy of Life Sciences' to open in April 2004. The £8 million Academy will provide the opportunity for innovative cross-disciplinary work by the integration of clinically related research in neuroscience. It will include research groups working on behavioural and cognitive sciences, neuroimaging, vision, ophthalmic and physiology optics.
54. The National Anti-Vivisection Society and Lord Dowding Fund submit that, before considering over-ruling strong local public opposition to this laboratory, the Public Inquiry and the Secretary of State should seriously consider whether a facility to house primates is the kind of research which is in the public interest.

Section 2. Differences between non-human primates and humans

55. A summary of evidence, and discussion of species differences. Experience has shown that both behavioural neuroscience and other neurological experiments on animals are fundamentally flawed due to species differences. For example:
 - The physiological (the functional reactions in the body) response of an animal to a painful or distressing stimulus varies not only between species but between individuals and is determined by the genetic makeup of an animal¹. Non-human primates, despite their evolutionary closeness to us, are distinct from us in the way they express genes in the brain. There are even big differences in gene expression between humans and chimps, although gene expression between chimps and other non-human primates is similar².

Species Differences

- Another hurdle when using animals to model human nerve diseases (or any other disease for that matter) that has not been overcome is that the human form of the disease can never be completely replicated in an animal. Animal models of the neurodegenerative disease Alzheimer's, for example, do not develop the characteristic 'neurofibrillary tangles' or show significant neurodegeneration³.
- It is unlikely that progress will be made in the study of the human brain by using laboratory animals, even species like macaques which are supposed to closely resemble humans. As researchers at two prestigious institutions, the Salk Institute and the University of California wrote: *"What is known about the neuroanatomy of the human brain? Do we have a human cortical map corresponding to that for the macaque? And what does the human equivalent of the connective map look like? The shameful answer is that we do not have such detailed maps because, for obvious reasons, most of the experimental methods used on the macaque brain cannot be used on humans. For other cortical regions, such as the language areas, we cannot use the macaque brain even as a rough guide as it probably lacks comparable regions"*¹⁹.
- Parkinson's disease is unique to humans²⁰, slowly progressing, whereas MPTP-induced Parkinsonism is rapid in its course. There are differences in nerve degeneration and the transmission of nerve impulses in naturally-occurring human Parkinson's disease and MPTP-induced Parkinson's disease in animals²¹. Also, there are major differences at both the behavioural and neurochemical (nerve chemistry) levels between marmosets and cynomolgus monkeys when administered MPTP, which draws the conclusion that results of macaque and marmoset experiments would be unreliable if applied to humans²².
- In 1999 the Animal Procedures Committee (APC) voiced concerns about the use of macaques in MPTP-induced Parkinson's disease. One reason was due to the differences in brain architecture between human beings and macaques, raising doubts about the transferability of results (although the project licence was granted anyway)²³.
- There are species differences between MPTP-induced Parkinson's in marmosets and human Parkinson's patients; the absence of Lewy bodies (as seen in Parkinson's patients) in marmosets²³. In the past, researchers gave a poor reason for using marmosets ie their small size. Now they are saying their brains are too small¹⁷.
- Human brains have a folded cerebral cortex (a gyrencephalic brain) whereas smaller primates, such as the marmoset, have a smooth cerebral cortex (a lissencephalic brain). Not only are there anatomical differences between a gyrencephalic and a lissencephalic brain but evidence suggests that there are functional differences, too⁴⁷.
- Lower and higher primates differ from one another by a number of structural features in their nervous systems and sense organs. The brains of lower primates are much smaller in relation to body size than those of the higher primates. The association areas, which govern the transfer of information between the different brain centres, differ in development between brains of higher and lower primates⁴⁸.
- The role of the hippocampus in human memory was complicated for a time by findings from behavioural studies of monkeys and other animals with hippocampal lesions, until its role was established in 1986 from a case of amnesia which developed in a human patient who had sustained brain damage⁴⁹.

- The chimpanzee brain is about one quarter the size of the human brain and the macaque brain is around one quarter the size of the chimpanzee brain. Comparisons between the human brain and that of non-human primates are limited by the greater complexity of the human brain, due to its larger size, and exemplified by its unique capacity for language. Although there are counterparts of the macaque brain's structures in the human brain, their functions may have diverged over the course of evolution⁵⁰.
- Often, areas in the brain that appear to have a function in monkeys do not have the same role in humans⁵¹.



Section 3. Is a primate facility sustainable in the long-term?

56. It has been stated that the proposed primate laboratory will fulfil a national need. Even proponents of the plan would have to describe this as highly speculative. We have outlined in the previous sections different scientific approaches in the field and problems with extrapolating non-human primate data to humans. In addition, there are other external factors likely to impede the functioning of such an establishment – not least a ready supply of primates. This is, by any standard, a risky investment.

The future of neurological studies on primates

57. Between 1990 and 2001 (the most recent government statistics available) there was a 25% drop in the total number of primate experiments, from 5,284 procedures to 3,986. Because some animals are used for more than one experiment, this does not necessarily correlate to the total number of primates used. In 1990 3,630 primates were used, dropping by 8% to 3,342 in 2001, indicating a shift from primate experiments, despite similar numbers of the animals being available⁵².
58. By increasing their use of primates, Cambridge University would be going against this overall national trend.
59. Since 1995, the Home Office has supplied statistics for the use animals in experiments concerning the central or peripheral nervous systems (these were reproduced prior to this, but with a slightly different classification). Macaque experiments in this field have been relatively stable, with the exception of unusually high usage in 2001, averaging 377 animals per year. 2001 shows that UK lab capacity can operate well above (22% above) the average annual national usage⁵².
60. 1995: 382 experiments on macaques⁵²
1996: 363 experiments on macaques⁵²
1997: 407 experiments on macaques⁵²

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1998: 336 experiments on macaques⁵²
1999: 400 experiments on macaques⁵²
2000: 294 experiments on macaques⁵²
2001: 461 experiments on macaques⁵²

61. Given that these figures are for “all nervous system research” across the UK it shows how a large new facility will dramatically expand this field of research, but this expansion is planned without any apparent demand in this particular field.
62. With finite numbers of primates available (see later), and limited research funds, one wonders if the facility may simply draw research away from other UK primate laboratories. Good news for Cambridge University perhaps, but hardly fulfilling a national need.
63. Primate research will be competing for funds with non-animal research, which given the recent dramatic steps forward in this field, is likely to be a fierce competitor for funding of projects.
64. Studies which might have been deemed too invasive for human subjects a decade ago, are now available with the latest non-invasive scanning technologies (see first section). That the Cambridge primate laboratory might draw funding away from leading edge non-animal research, where the UK is currently at the forefront, must be cause for concern.
65. Primate research will also be under pressure from developments within the animal experimentation field itself. The major growth area in animal experimentation is the use of genetically modified animals, which commentators from both the animal research and anti-vivisection communities are in agreement, looks set to continue growing. Whilst the NAVS has clear scientific and ethical criticisms of such work, it is apparent that within the coming years, a considerable amount of animal research (if not the majority) will shift from using conventional animals to genetically modified animal models of human disease. In the absence of any indication that such fields of research will be excluded, it is reasonable to expect that models will be designed for diseases such as Alzheimer’s and Parkinson’s⁵².
66. The scientific community also agree that for the foreseeable future research on genetically modified animals will involve rodents and not primates.
67. In 2001, 179,846 procedures were conducted on genetically normal animals in order to produce or breed GM or mutant animals with a harmful modification. In the production of genetically modified animals, no primates were used. In total, in 2001, 630,759 procedures were conducted on genetically modified animals – none of these were primates. This already represents almost a quarter of all procedures on animals in the UK and the figure has risen steadily since 1995⁵².

68. Given such developments, it seems an extraordinary time to propose the expansion of a primate laboratory for neurological studies.

69. It would not be the first time that an area of animal experimentation has expanded rapidly on a promise, and for that promise to be left unfulfilled: In the late 1980s in the US in response to fears about AIDS, there was a rush to animal-based AIDS research. Expensive laboratories were filled with expensive chimpanzees, but the research effort followed a different course. The legacy was a huge financial burden, and an animal welfare crisis, for the chimpanzees stuck in the laboratories.



70. In 1997, a panel at the US National Academy of Sciences reported that a \$7 million Chimpanzee Management Program (or ChiMP) should be established to provide lifelong care for over 1,000 research chimps in the USA. The cost of this programme would be similar to that being borne by government agencies already holding surplus chimps. The panel also proposed a four year moratorium on chimp breeding⁵³.

71. Despite that it is often claimed that there is increasing demand for animal research, it was reported in 2000 that the Coulston Foundation of Alamogordo, New Mexico was heading for financial crisis, having lost two contracts to house HIV-infected chimpanzees and undertake experiments on them. With private funding also drying up, 20 employees at the facility, which at the time held 620 chimpanzees and 250 monkeys, were laid off⁵⁴. The Florida-based Center for Captive Chimpanzee Care has recently bought the facility. The freedom of the remaining 266 chimpanzees and 61 monkeys, many of which had been used for HIV and hepatitis research, is thanks to a generous \$3.7 million donation from the Arcus Foundation in Kalamazoo, Michigan⁵⁵.

Existing difficulties in primate supply

72. Laboratory primates, particularly macaque monkeys, are expensive and supplies are finite.

73. The number of macaque monkeys being used in UK laboratories has remained relatively stable between 1990 and 2001, with 2,065 and 2,219 animals respectively⁵².

74. In 1995, documents uncovered by the NAVS indicated the difficulties experienced by London's Institute of Neurology, in trying to obtain these animals⁵⁶.

75. On 24th August, 1994, J.L. Frogley, Superintendent of the Denny-Brown Laboratories, Institute of Neurology, wrote to the Home Office Inspector: *"...to apply for an exemption certificate to enable us to import three rhesus monkeys employing a broker and not a*

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*designated supplier. The animals which are captive bred, will be used by Prof. E.P.G.H du Boulay under the authority of Project Licence number PPL 70/03439. 'Our initial order has been placed with B & K Universal Ltd., and the animals would come from their breeding station in China. I cannot at this time provide a definite delivery date as the suppliers are experiencing difficulties with the airlines over the transport of live animals. As soon as this is known I will inform you.'*⁵⁶

76. On 19th September, 1994, he wrote again pressing his request. *"I have in fact approached Shamrock Farms and learned that they too import from China and are experiencing difficulties with shipping the animals to the UK. I have also approached the Institute of Aviation Medicine and UMDS (Farnborough, Hants - reported as having a Rhesus breeding colony in 1981), neither of which have animals the size we require. Through an intermediary, HRC (Huntingdon Research Centre, Cambridgeshire) have been contacted and have nothing to offer. Bantin and Kingman Universal have themselves also contacted establishments in the UK to no avail. Whilst the odd animal is available they do not meet the critical size requirement needed in order to carry out the procedure"*⁵⁶.
77. Primate supply has grown increasingly difficult, rather than easier. Whereas with almost all other species the shift has been towards breeding the animals on site, with the primates, particularly macaques, animals are purchased, in the main, from outside suppliers. Despite an apparently strong market, the demand has not been enough to sustain a UK-based supplier. The last UK supplier, Shamrock Farms, closed in the summer of 2000⁵⁷.
78. In the Statistics of Scientific Procedures on Living Animals Great Britain, 2001, the Home Office notes, *"the recent closure of the main non-human primate supplying establishment has resulted in more project licence holders sourcing such animals directly from abroad"*⁵².

General restriction of primate usage

79. There is considerable public concern about the use of animals in research, particularly the use of primates, due to their closeness to humans in terms of intelligence, developed social structures, forms of communication, and even use of tools.
80. Added to this are grave concerns about conservation of primate species in their range states; the laboratory primate trade has added to the pressures on wild populations.
81. Thus, it is expected that in the coming years the use of primates in experiments is one of the most likely areas where tighter regulation and control, either nationally or even internationally, will be seen.
82. In 1994, the Home Office accepted a recommendation from the Animal Procedures Committee (APC) that: *"The use of wild-caught non-human primates should be banned except where a project licence applicant can establish exceptional and specific justification"*⁵⁶.

83. Lady Blatch, on behalf of the Home Office, reported to the APC, *“The Home Secretary welcomes your advice that the use of wild-caught non-human primates should be banned except when exceptional and specific justification can be established and accepts the Committee's recommendations which will underpin the ban. He believes that they will ensure public confidence in the arrangements for controlling the source of supply of captive-bred animals⁵⁶.”*
84. Public disquiet has resulted in more detailed guidelines for primates in the government's “Code of Practice for the Housing and Care for Laboratory Animals” (COP) than for any other species⁵⁸. To date there is little evidence of effective enforcement of the COP. In two candid studies of primate by the NAVS inside St Mary's Hospital Medical School and the Institute of Neurology, both in London, almost every primate husbandry guideline was routinely breached⁵⁶.
85. At some stage the Home Office will have to enforce the standards of husbandry it has already set, and indeed raise these to a level that might be acceptable to the public.
86. Furthermore, it is not unreasonable to expect the licensing of animal experiments to be reviewed, especially in regard to primates, as there is evidence of the severity of procedures being understated, and conditions of licences and regulations being ignored⁵⁶.
87. In addition, because the majority of animals (imported macaques) endure extremely long journeys from their country of origin (longer than recommended for livestock under EU regulations), animal welfarists have proposed classifying all procedures for these animals in the ‘substantial’ suffering category, thus requiring greater justification for their use.
88. In short, one would expect it to become increasingly difficult to get permission to conduct experiments on primates.
89. In addition to the potential for restriction from the UK government, the Cambridge facility will be at the mercy of its foreign suppliers; carriers; national legislation, and even the political climate in countries forming part of the primate species' natural range.
90. In 1978, the world's main supplier of rhesus macaques, India, banned the export of the animals and laboratory primate use shifted from rhesus macaques to cynomolgus macaques. As wild populations of these species diminish, other countries are expected to consider such options⁵⁹.



Jan Cremer / NAVS

Conclusions

Health & Safety & potential restrictions to primate trade

91. Primates carry a range of diseases which can be harmful, even fatal, to humans. The herpes simian B virus, which can infect macaques, is a classic example of a virus that can be dangerous to humans once out of its host species⁵⁹. In December 1997, a primate researcher at Yerkes Primate Research Center in the USA died after infection with Herpes B virus, transmitted through her eye. The woman, who was wearing full protective clothing, except eye protection, felt a sting in her eye while moving a caged rhesus monkey. The eye became inflamed ten days later and four weeks after this she was dead⁶⁰.
92. Marburg Disease takes its name from the town in Germany where the first outbreak took place. Twenty nine laboratory workers became infected, suffering high fever, slow heart rate, headaches, inflammation of the eyes, stomach aches, vomiting, diarrhoea, and prostration. Seven died. The researchers who first contracted the virus had been exposed to tissues or cell cultures from recently imported African green monkeys⁵⁹.
93. Aside from concerns that a primate pathogen might escape the Cambridge facility, such disease problems lead to periodic disruption of supplies of laboratory primates.
94. In 1989 the US authorities in New York State banned all imports of cynomolgus, rhesus and African green monkeys when it was suspected that cynomolgus macaques supplied from the Philippines were infected with the lethal Ebola virus. It transpired that they were infected with another strain of filovirus (named Reston Strain Filovirus after the location of the primate facility in Reston, Virginia where it was first discovered). Then in 1996, two cynomolgus monkeys from the same Philippines' source were found positive for the filovirus at HRP, Inc. in Alice, Texas. The Philippines government banned the export of monkeys, only lifting the ban after tests showed animals at most facilities were not infected with the filovirus; one facility holding animals infected with the "Reston" virus subsequently closed^{61,62}.

Summary and conclusions

95. The National Anti-Vivisection Society and the Lord Dowding Fund for Humane Research submit that the proposed primate research facility is not in the national interest owing to the following considerations:
96. World class science is in the field of non-animal research. An example of this may be found in the plans for a Neurosciences Research Institute at the University of Aston in which an environment fostering cross-disciplinary work by integrating clinically based human research in neuroscience has been proposed. A centre of excellence for neuroscience research is possible without animal experimentation.

Conclusions

97. Neurological research involving animals is fundamentally flawed owing to species differences, presenting insuperable obstacles to the extrapolation of data from animal experiments to the human situation. Even the Animal Procedures Committee, the statutory body set up to advise the Home Secretary, has voiced concerns about the differences of brain architecture between humans and macaques and the consequent difficulties in transferring results from such experiments to the human situation. Human forms of neurological disorder cannot be completely replicated in an animal and drugs based on these animal models of disease are not guaranteed to treat it successfully in humans. Hence the facts do not bear out the claim that medical and pharmaceutical research will benefit from the initiative of the kind proposed by the University of Cambridge.



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98. Modern sophisticated imaging techniques are more efficient and revealing and can be used in patient studies and with other human volunteers. Such techniques overcome the problem of species differences. Hence the advancement of our knowledge of the human brain/mind is better served by facilities for further progress in such areas.
99. The UK is currently at the forefront of leading edge non-animal research and, given finite resources, the proposed centre would draw funding away from such research areas.
100. The trend in animal research does not support the argument for an expansion of primate research. The growth area in animal experimentation is on genetically modified animals, an area which for the foreseeable future will involve rodents not primates. Moreover there has been a drop in the number of primate procedures in the UK, while macaque experiments in particular have remained stable, indicating there is no apparent demand for an increase.
101. The use of primates presents special long-term difficulties within the field of animal experimentation. Supply has grown increasingly difficult, and has put pressure on wild populations leading to concern over conservation. Meanwhile the special concern of the general public over the issue of primate experimentation has led and will continue to lead to increasingly tighter regulation, the rigorous enforcement of which will make it increasingly difficult to get permission to experiment on primates and to comply with the regulations for doing so. Also primate species carry a range of diseases which can be harmful, even fatal, to humans.

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