The end of monkey research?

New legislation and public pressure could jeopardize research with primates in both Europe and the USA

Kevan A. C. Martin, a neurobiologist and director of the Institute of Neuroinformatics—a joint institute of the University of Zurich and the Swiss Federal Institute of Technology—has a moral dilemma. For the past four years, he has not hired any postdoctoral fellows or PhD students. He feels he cannot take them on in good conscience because he cannot guarantee they will be able to do research. It was another moral debate that put him in this position; his work on rhesus macaques has been put on hold and he is uncertain when, or if, it will resume in Switzerland.

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In 2004, the Swiss Constitution was changed to acknowledge “the dignity of living beings,” which, according to Martin, was intended to address concerns about transgenic experimentation, rather than animal research in general. Nevertheless, the change resulted in some members of a local external advisory committee on animal experimentation legally challenging the 2006 renewal of Martin’s license to use the monkeys for neurobiological research. Similar legal action was taken against Daniel Kiper at the same institute, whose research on brain plasticity in monkeys has relevance for stroke patients. A third researcher, whose work on motor systems has implications for patients with spinal cord damage, has decided to leave Switzerland (Staub, 2007). All three of these projects were approved by the Zurich Canton’s Veterinary Office, which controls

experiments on animals. Martin’s case has been working its way through the Swiss courts and is finally before Switzerland’s Federal Supreme Court. In the meantime, Martin, who established the Institute in Zurich with Rodney Douglas 13 years ago, has been limited to using post-mortem monkey brains.

These are just some examples of the impact that the growing international animal rights movement is having on research, and the legislative momentum is continuing to build. While the widely publicized passage of a resolution by the Spanish Parliament to extend human rights to higher apes, and California’s Proposition 2 to improve conditions for farm animals are two further examples, the real impact on primate labs might come from pending revisions to legislation in Europe and the USA that could potentially end research on apes and monkeys altogether. If that happens, researchers fear there would be serious consequences not only for basic science but also for medical research.

Even now, Swiss scientists are not alone in having their work stopped by legal challenges. Andreas Kreiter, a brain researcher at the University of Bremen’s Center for Cognitive Science in Germany, uses macaques to study neuronal brain patterns to try to understand perception. Despite approval from the federal authorities and the agency funding his work, Bremen’s State Senator for Health stopped the research on the grounds that it was “ethically unjustified” (Estrella, 2008). Like Martin, Kreiter is fighting the ruling in court with backing from the university.

“As the independent UK Weatherall Report on the use of non-human primates in research reported, macaques are an important model,” Martin noted (Weatherall, 2006). “The macaque monkey

is an old-world monkey and it is the most similar, in terms of behaviour and brains, to humans, unlike new-world monkeys.” As a result, he explained, his research is an essential step towards understanding the neural basis of many human neurological diseases. “The ethical discussion is essential, and which way it goes has huge consequences, especially for humans,” he said. “If you want to take away the means to do the kind of research that leads to a fundamental understanding of the brain’s circuits in health and disease, then in the long-term that is going to have a negative effect on human mental health and welfare.”

Beyond these local court cases, it is the revision of the European Union’s (EU) Directive 86/609 on the protection of animals used for experimental and other scientific purposes that is going to have the biggest impact on primate research in Europe. Efforts to update 86/609 have been under way since the European Parliament requested a revision in 2002 to harmonize standards between the EU member states and make the directive more enforceable. The Swedish Presidency has fast-tracked the revision but the final terms are not yet known as the Council of Ministers and the European Parliament continue to work out a new text.

The revision of 86/609 worries supporters of animal research, especially about how it will affect macaque research

The proposed changes call for, among other things, limiting research on primates to work that is related to the “prevention or treatment of life-threatening or debilitating clinical conditions in human beings”;

limiting research on primates to those bred in captivity for two generations, so-called F2 animals; applying the F2 requirement to marmosets immediately and to cynomolgus and rhesus macaques within seven years; and banning research on great apes. However, there is a “safety clause” to authorize the use of great apes for research that is considered critical to preserve the species or in relation to an unexpected outbreak of a life-threatening disease (http://ec.europa.eu/environment/chemicals/lab_animals/proposal_en.htm; http://www.ecbr.eu/directive-86,609_2.htm).

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The revision of 86/609 worries supporters of animal research, especially about how it will affect macaque research. “It is very difficult to see how fundamental research would be permitted,” commented Mark Matfield, general secretary to the European Coalition for Biomedical Research—a coalition of academic associations and institutes in the biomedical sciences. “A lot of fundamental neuroscience is done on macaques.” He also expressed concern about limiting researchers to F2

macaques. “Many of the macaques used in research anywhere in the developed world are bred in captivity, but are the first generation,” Matfield said. “No one knows if it is possible to breed enough second-generation macaques.” He added that there are not enough F2 animals to keep research at its current level, which might mean that the research would move to China or other countries, where the conditions for laboratory animals might be worse than in Europe. The European Commission declined to comment on the topic.

Some EU member states, regardless of any revisions to 86/609, are attempting to improve the rights that animals are granted under their own laws. In June 2008, Spanish legislators passed a non-binding resolution stating that all great apes, including chimpanzees, gorillas and orangutans, should be entitled to the rights of life and freedom. As such, the resolution called for an end to experimentation on great apes for the sake of science because it would never be permitted with a human subject.

However, Matfield remains unimpressed. “In a sense, what the Spanish did was just an empty gesture,” he said. “They certainly did not pass something which gave great apes legal rights the way humans have them [...] they did not make them subjects of the law in their own life, the way human beings are.” Still, Matfield thinks it is likely that the USA will become one of the last countries

to allow research on apes. “In a sense, the whole question about the use of great apes is a non-issue [in Europe], I mean it’s finished, it’s not going to start again,” he said. “No national government would approve it in the European Union.”

In passing their resolution, Spanish legislators have upheld the principles of the Great Ape Project (GAP; São Paulo, Brazil), which is supported by an international membership of primatologists, psychologists, ethicists and others, who are calling for laws to promote legal rights for great apes. According to many scientists, great apes have the mental capacity of a human child and experience emotions such as happiness and depression. Michele Stumpe, president of GAP International and North America, commented that it does not make sense that great apes do not have basic rights already, especially given the extensive similarities between apes and humans. She explained that chimpanzees, for example, share many human emotions. “They mourn, they laugh, they cry, they have social groups, they plan for their futures,” she said. “It makes it easy to objectively state that there are certain qualities that most humans would deem morally significant.”

Peter Singer, Professor of Philosophy at Princeton University (Princeton, NJ, USA), who is considered the father of the animal rights movement and is one of the founders of GAP, said he is not surprised by the current paradigm shift. “There is certainly

a genuine movement of increased awareness and increased concern for animals that is occurring in many countries," he said. "There are even signs of great ape movements in countries that have not traditionally shown concern for animals."

Singer, who wrote the 1975 book *Animal Liberation*, a rallying cry for rights and protection for animals, said that the animal rights movement has shifted away from the image of protestors splattering blood on fur coats or disrupting animal laboratories, and into the political realm. He is, therefore, pleased with California's Proposition 2, which establishes that farm animals are entitled to sufficient room for roaming. "I think that [passing this referendum] shows is that the American public as a whole is supportive of at least getting rid of the worst forms of factory farming," Singer said. "I think that's where by far the largest amount of human inflicted animal suffering is." He also added that he believes the ball is rolling on animal rights much faster than expected, pointing out that more Californians voted for Proposition 2 than voted for Barack Obama, who is very popular in the state, to become president.

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Indeed, the US Congress might soon establish legislation to reduce the amount of research conducted on primates. Representative Roscoe Bartlett, a Republican from Maryland, has introduced a bill that would require researchers to substitute invasive research on great apes with existing alternatives. Bartlett himself was unavailable for comment because Congress was out of session, but Lisa Wright, a spokeswoman for him, explained that the congressman is disgusted with the treatment of some of humanity's closest relatives. "Science has progressed sufficiently with tissue typing and other techniques that it is no longer necessary to utilize [...] primates, who are extremely intelligent and social animals," she said.

Yet, the passage of the bill is not a done deal. According to Justin Goodman, the research associate supervisor for People for the Ethical Treatment of Animals (PETA;

Sidebar A | Further coverage of the ethics of animal research

In *EMBO reports* (June 2007), see the Talking Point on the topic:

Animal rights, human wrongs?

Frank Gannon
EMBO reports 8: 519–520

Animal research: a moral science

Bernard E. Rollin
EMBO reports 8: 521–525

The ethics of animal research

Simon Festing & Robin Wilkinson
EMBO reports 8: 526–530

Norfolk, VA, USA), getting laws passed for animals, even for apes, is very difficult in the USA because of a lack of public understanding of the plight of these animals. "We have no legislation for great apes right now, so it's hard to imagine giving protection to other non-human primates who people perceive to be even more different to humans anytime soon," he explained. "Because the legislation process is so slow going, we spend most of our time related to primate experimentation issues educating the public about the utter tragedy that these social and intelligent animals are being locked in cages and driven mad by confinement."

Notwithstanding the process, Bernard Rollin, a bioethicist at Colorado State University (Fort Collins, CO, USA) and principal architect of 1985 US legislation dealing with the welfare of experimental animals, said it has taken people long enough to stand up for animals. Yet,

he also anticipates that primates will eventually be exempt from being research subjects. "I suspect that primate research will slowly disappear because people have a special thing about primates," he said. "I've heard researchers say they hate doing stuff with monkeys because they're people in monkey suits."

While the debate continues around the world, Martin and his macaques must continue to bide their time. "What I've discovered with the legal process is that it is achingly slow [...] [it has been more than] three years since my experiments were stopped, and I still don't have an answer," he said. "This has had a major negative impact on my own contribution to this important field of research, but if I were a young researcher, it would also have had a devastating impact on my training and my career prospects." For now, the balance between the rights of animals and the needs of medicine and science is neither obvious nor easy.

See Sidebar A for further reading.

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The secret garden

The human digestive system is teeming with microbiotic life, but just how important are these interlopers for health and disease?

A vast number and variety of bacteria enjoy the warm and nutrient-rich environment of the human gut. Some of them are pathogens, whereas most others could be mistaken for simple hitchhikers along for the ride. Yet, it has become clear that the hitchhikers are actually paying their way; indeed, the extent

of our dependence on these extragenomic microorganisms, or microbiota, for health is remarkable. The insight that our gut flora have an enormously important role in nutrition and disease has given rise to the term 'microbiome' to describe loosely all those microbial genes—and their products—that interact with our own genome