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Still prime time for primates

Rats turn out to be surprisingly useful for research on cognition. But if the goal is to understand the human brain and its many disorders, then primate studies remain essential.

Researchers who study cognition in non-human primates have long had to contend with protests from animal-rights activists, who argue that experimenting on such close human relatives is ethically abhorrent. Now a wave of research showing that some cognition experiments can be carried out in rodents (see page 282) has given scientists something else to worry about. Will activists try to exploit these developments to argue that there is no longer a scientific justification for using primates?

Even the most enthusiastic proponents of rodent-cognition research share this worry. They have had to argue hard to convince some people within the scientific community that useful work can be done in rats — and some sceptics remain unconvinced. But the rodent researchers have never argued that rats could or should replace primates in research that is ultimately directed at understanding how the human brain works — and thus what goes wrong in neurological and psychiatric conditions.

What these scientists have discovered over the past decade or so is that rats can do simple cognitive tasks that had often been assumed to be beyond them and that, with appropriate training, they can indicate what is going on in their minds by poking their noses in different directions. In retrospect, this is perhaps not so surprising. After all, rodents in the wild have to navigate safely and successfully in constantly changing environments, just as primates do. Because the brain is the organ that has evolved to fulfil this task, the basic mechanisms for cognitive functions such as remembering, paying attention and discriminating certain stimuli are likely to have been conserved across evolution.

This approach — combined with the low cost of rearing and keeping rodents and the wide availability of genetic tools for studying them — promises to help scientists to reach these basic cognitive components with unprecedented speed and rigour. Rodent research is also a less ethically sensitive issue than primate research, so the more information that can be wrung out of rats and mice the better. However, scientists will not be able to extrapolate directly from the rodent brain to the human brain to work out what has gone wrong in complex disorders such as schizophrenia. Nor will rodents do much to help scientists develop neuroprosthetics that may one day help to compensate for loss of brain tissue. Structurally, the brains of rodents and humans are just too different.

The human organ has a large, highly evolved outer layer — the cortex — that provides a processing power unequalled in the animal world for making sense of external stimuli. Included in this layer, situated right behind the forehead, is a pronounced prefrontal cortex where thoughts are orchestrated and complex plans are formulated. Rodents, by contrast, have a minimal cortex and no prefrontal cortex. Their brains accordingly cannot help to illuminate the additional levels of complexity of functional brain networks in humans.

"Non-human primates have a level of social intelligence that is missing in rodents but highly relevant for humans."

The brains of non-human primates are anatomically closer to those of humans, so their cognitive strategies are more likely to be similar. Non-human primates also have a level of social intelligence that is missing in rodents but is highly relevant for humans. The empathy between primates allows them to form complex social bonds — and perhaps underlies the human instinct to protect monkeys and apes.

Rodent studies have the potential to deliver reliable data that can inform human, and primate, cognition research, and allow those experiments to become even more revealing. But, if the goal is to understand the human brain and mind, rodent and primate work will need to be continued in parallel for the foreseeable future. It's a no-brainer. ■

Change of purpose

The United States should protect investments used to find new uses for old drugs.

In 2007, a paper in the journal *Cancer Cell* announced that the compound dichloroacetate (DCA) had been found to shrink tumours in rats (S. Bonnet *et al. Cancer Cell* **11,** 37–51; 2007). That news by itself would not have created much of a stir: many compounds tested in rodents raise hopes of their becoming potential cures, and almost as many go on to fail in human clinical trials. But DCA had already been tested in humans against a condition called lactic acidosis, and so seemed to be relatively safe. Indeed, the authors of the paper argued that DCA could swiftly find its way into late-stage clinical trials against cancer — except for one problem. The drug was no longer protected by patents, and no pharmaceutical company would invest the millions of dollars needed to fund clinical trials.

Since then, the researchers have managed to pull together enough funding for preliminary trials, the first of which was published last week (E. D. Michelakis *et al. Science Transl. Med.* **2,** 31ra34; 2010). Supported by a mix of Canadian federal grants and donations from philanthropic organizations and individuals, the study showed promising results when DCA was used against a form of brain cancer. But the team was able to test the drug in only five patients. And although the researchers have gathered enough funding for additional small studies, they admit that the prospect of moving into the final phase of clinical testing — which typically involves a much larger trial — is daunting.

Over the past few years, as observers have lamented the declining