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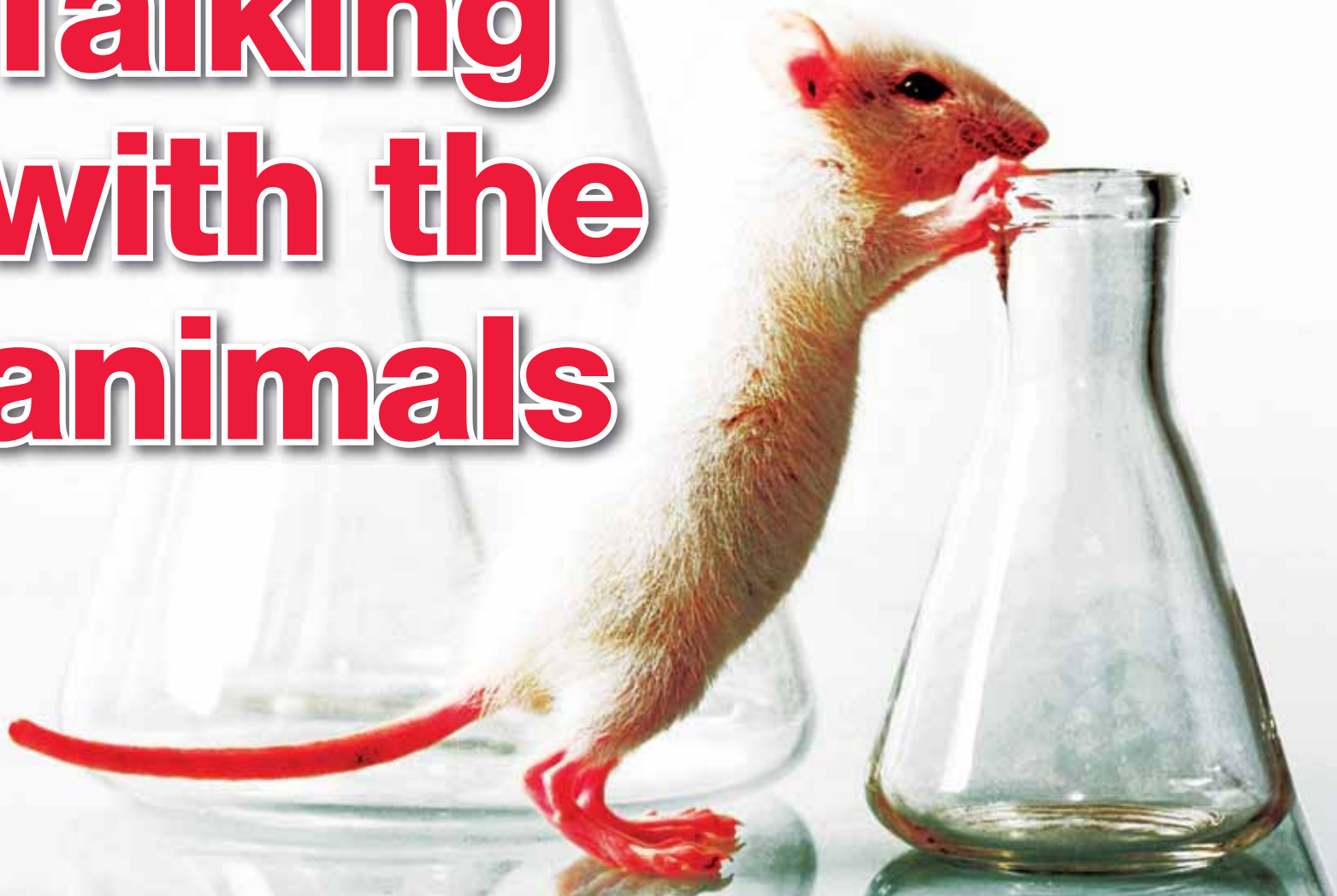
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# Talking with the animals



New resources are allowing *in vivo* scientists and animal technicians to improve the welfare of their laboratory animals and subsequently benefit the outcome of their experiments

A quiet revolution is taking place within laboratory animal facilities all over the world. The latest findings from the multidisciplinary field of animal welfare science are being brought to bear on the lives of the many millions of mice, rats and other animals used in research to advance biological knowledge and understand and treat disease. Ground-breaking methodologies now allow scientists to ‘ask’ animals how they feel about the conditions in which they are kept and the procedures that they undergo, what they value and want in their environment, and whether they are in pain. And the appetite to act on this new information about animal sentience is increasing. The potential to transform laboratory animal welfare is huge.

Why does this matter? Well clearly it’s important from an ethical standpoint – it’s morally right to improve the quality of life of the animals in our care. But it’s also important from a public perspective – opinion polls of attitudes to animal experimentation repeatedly show that public support is conditional on the adoption of high standards and the prevention of unnecessary harm to the animals. So demonstrating a commitment to the welfare of research animals, and to avoiding or alleviating any pain, suffering or distress they might experience, should help garner further support for animal-based experiments where they remain necessary and justified. But perhaps what is really causing a change in attitudes and research practices is the increasing realisation that failure to address the welfare needs of laboratory animals can compromise the scientific quality, and perhaps even the validity, of the research for which they are being used. The evidence base for this proposition is growing and it’s a real wake-up call for scientists.

Take for instance the simple act of handling a laboratory mouse – an unavoidable part of most research procedures using

this animal. The traditional and widespread method, recommended in most text books, is to pick up the mouse by the base of the tail and then to place it on a surface, such as the cage lid or the opposite hand, from where it can be restrained by the “scruff” (the loose skin of the neck) for taking, say, a blood sample. However, prize-winning work<sup>1</sup> by Jane Hurst, Professor of Animal Science at the University of Liverpool, has shown that this method of handling causes high levels of anxiety, which can influence experimental outcomes. Even after multiple handling sessions, mice picked up by the tail avoid approaching the handler, show high levels of urination and defecation during handling, and exhibit high avoidance of open spaces in the elevated plus maze – a test of anxiety. By contrast, alternatives such as scooping up the mice in a “cupped” hand, or allowing them to walk into a clear plastic tunnel and using that to transfer them to the hand, lead to voluntary interaction with the handler, much lower levels of anxiety and greater acceptance of physical restraint. The difference in behaviour is seen clearly in the supplementary movies that accompany the online version of Professor Hurst’s paper in *Nature Methods* and challenges preconceived notions of what is normal behaviour in response to handling. What’s more, cupped and tunnel-handled mice show less variability in their response to handling, so there is real potential here to reduce unwanted variation between animals and laboratories, which is currently uncontrolled. This could increase the sensitivity of experiments and reduce the number of animals needed for research.

“If universally implemented, these small changes in handling, which are easily applied, will benefit every mouse used in research – and that’s tens of millions of animals. Picking up mice in a tunnel is a particularly effective way to habituate animals to handling that they find non-aversive. It is a very quick and practical method for picking mice up or transferring them ▶



The Procedures with Care website focusses primarily on manual skills needed, including subcutaneous, intravenous, intramuscular and intraperitoneal injection. © Newcastle University



cages that takes no longer than the standard tail method and a number of large animal facilities are now starting to adopt this. We've also found that mice handled this way show more confident exploration when removed from their cages, so show reliable responses in cognitive behavioural tests," says Professor Hurst.

It was recognition of the importance of good animal welfare for good quality science, as well as concerns about the limitations of animal models, that led the UK Government to establish in 2004 the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) – a scientific organisation pioneering better science through the application of the 3Rs: replacement of animals with non-animal alternatives, reduction of the number of animals used, and refinement of procedures and husbandry to minimise suffering. The Centre has rapidly become a global information resource on the 3Rs and the main funder of 3Rs research in the UK. It funds across all three of the 'R's and the spectrum of scientific disciplines – from oncology, through neuroscience, to toxicity testing – but around one fifth of its grant awards by value (£6 million) are for projects aimed at avoiding or alleviating pain and other adverse effects in laboratory animals. "Animals will remain an essential part of bioscience research and drug development for some time to come, so it's important that the third 'R' – refinement – is given due attention. We've successfully engaged leading research groups to develop novel means of measuring animal welfare and to refine models and practices to reduce suffering," says Dr Vicky Robinson, NC3Rs Chief Executive.

**A major recipient of NC3Rs** research funding is Newcastle University's Pain and Animal Welfare Sciences (PAWS) group, which is recognised internationally as a centre of excellence in this area. The group is currently investigating methods for alleviating pain in mouse models of cancer, assessing the suffering of macaque monkeys used in neuroscience studies, and refining gaseous euthanasia of rodents to address concerns about distress before loss of consciousness. A recent award to Dr Matt Leach, Lecturer in the School of Agriculture, demonstrates one of the many innovative approaches being taken by the group to tackle the challenge of reliably identifying pain and quantifying its severity

in animal subjects who, of course, can't tell us directly how they feel through speech. Dr Leach explains: "Traditional methods of pain assessment in animals are often based on monitoring of weight loss, food and water intake, activity and clinical signs. These methods can be time consuming and may not always be specific to pain. The gold standard method for pain assessment in non-verbal humans, such as infants, is to use facial expressions, and we've been applying that to laboratory animals – most recently rabbits." Dr Leach and colleagues have developed the rabbit grimace scale<sup>2</sup> which is based on changes in a number of 'facial action units', such as narrowing of the eyes of the rabbit (orbital tightening), and bulging or flattening of the cheeks and nose. They have demonstrated that changes in these action units reliably indicate acute pain and correlate with physiological signs of stress, such as increased heart rate. It provides a new tool that could be used to improve the welfare of not just the hundreds of thousands of rabbits used in research worldwide, but also those kept as pets and as a source of meat.

The relationship between the NC3Rs and PAWS extends beyond funding primary research. Both have a strong track record in producing educational resources and training on best practice for *in vivo* researchers, veterinarians and care staff; for example on blood sampling – probably the most common procedure performed on research animals, anaesthesia and surgical skills and assessing animal health and welfare. In 2011 the two decided to collaborate, together with the Institute of Animal Technology – the professional body for animal technicians in the UK – on a new web resource on the administration of substances to laboratory rodents – another very common procedure. Professor Paul Flecknell, Head of PAWS and Director of the Comparative Biology Centre at Newcastle University said "We knew from experience that laboratory staff want practical guidance on how to administer substances to animals humanely and efficiently, and high-quality video was clearly the way to go." The resulting website, *Procedures with Care* ([www.procedureswithcare.org.uk](http://www.procedureswithcare.org.uk)), focuses primarily on the manual skills needed for subcutaneous, intravenous, intramuscular and intraperitoneal injection, as well as oral gavage. The video files and supplementary information is available for download as

## THE AUTHOR

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