INQUIRY INTO USE OF PRIMATES AND OTHER ANIMALS IN MEDICAL RESEARCH IN NEW SOUTH WALES

Name: Date Received: Dr Shaun Khoo, Dr Mike Kendig, Dr Laura Bradfield 20 March 2022

Animal Research is Saving Lives, but Funding is Needed to Improve Welfare

Shaun Khoo^{1,2}, Mike Kendig², Laura Bradfield²

¹ Department of Pharmacology and Physiology, Faculty of Medicine, University of Montreal, Canada. Present address: University of New South Wales, Sydney

² School of Life Sciences, Faculty of Science, University of Technology Sydney

SUMMARY

Many kinds of animal research are occurring in NSW, with biomedical research among the most prominent. As behavioural neuroscientists, we study the neural mechanisms of motivation and cognition in rodents, which is important for developing new treatments for a range of psychological disorders, such as substance use disorder, as well as neurodegenerative diseases such as Alzheimer's. The welfare and wellbeing of the animals we study is of critical importance, not only to ensure the quality of our data but to our sense of morality as compassionate human beings. Biomedical animal research is highly regulated and the pharmacological and biological tools we use pose negligible risks to the public. Meanwhile, our research brings enormous benefits to NSW by building expertise and supporting biotechnology companies.

Although research on complex behaviours cannot be replaced by non-animal procedures, we believe that there is much scope for refinement and improvement in animal welfare in NSW. For example, investing in a local breeding facility to produce animals used in NSW research projects would significantly reduce the stress associated with importing animals from interstate or overseas. Additionally, standard animal housing could be improved through targeted and ongoing investment to refit animal facilities and support additional caretaker and veterinary staff to provide higher degrees of welfare.

Background: Animal Research is Saving Lives

Virtually every single medical breakthrough that we rely on was developed using knowledge gained through animal research. Biomedical animal research has been absolutely critical to everything from uncovering basic biological functions to undertaking early tests of potential new therapies. Animal research provides a critical filter that removes the majority of unsafe or ineffective experimental therapies from the pipeline, precluding their use in clinical trials. In turn, this greatly reduces the likelihood of exposing healthy volunteers to health risks in early-stage clinical trials.

Perhaps the most obvious examples of how biomedical animal research is saving lives comes from the COVID-19 pandemic. A widely circulated study conducted in hamsters demonstrated that surgical masks could reduce the spread of COVID-19¹. This study was published in the early stages of the pandemic (in May 2020) and provided critical early evidence that COVID-19 spread through airborne routes. This finding was a key factor informing the introduction of mask wearing recommendations that have saved many lives in western countries. Similarly, in NSW over 95% of people aged 16 years and over have received at least one dose of a COVID-19 vaccine², which was tested in animals, including non-human primates³. Non-human primate studies continue to be essential, as pharmaceutical companies investigate the possibility of producing variant-specific boosters⁴.

In our research, we use animals to study the brain changes that underlie appetitive motivation, learning, reward, and cognition. Our research has contributed not only to the fundamental understanding of how the brain works but has guided the design of clinical studies for the treatment of psychological disorders, such as addiction. We are surrounded by colleagues who use animal models to advance the understanding and treatment of multiple sclerosis, Alzheimer's Disease, and numerous other diseases which have debilitating physical, psychological and emotional effects on ordinary Australians.

Animal Research is Highly Regulated and Negligible Risk

Animal research is highly regulated in NSW: any experiment proposing to use non-human animals is legally mandated to undergo review by an institutional animal ethics committee. These committees are designed to protect animal welfare and are legally required to include a veterinarian, a person with a demonstrated commitment to animal welfare, and a lay person. In fact, many institutions (including our own) try to go beyond the regulated minimums to ensure higher standards of animal welfare. In animal ethics applications researchers provide detailed explanations of their proposed experimental procedures; why these must be undertaken in non-human animals; and how any welfare concerns will be managed. Researchers must satisfactorily justify or amend procedures queried by the committee before approval is granted. Subsequent variations to approved ethics protocols must be similarly reviewed by the committee or a designated representative before they can be adopted by researchers.

¹ Chan et al. 2020. Surgical Mask Partition Reduces the Risk of Noncontact Transmission in a Golden Syrian Hamster Model for Coronavirus Disease 2019 (COVID-19). *Clinical Infectious Diseases*, 71(16), 2139–2149. <u>https://doi.org/10.1093/cid/ciaa644</u>

² https://www.health.nsw.gov.au/Infectious/covid-19/vaccine/Pages/default.aspx

³ https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-data-preclinicalstudies-mrna

⁴ Waltz 2022. Omicron-targeted vaccines do no better than original jabs in early tests. *Nature News.* <u>https://doi.org/10.1038/d41586-022-00003-y</u>

At any point during experimental procedures an ethics committee representative (or an individual external to the organisation) may inspect animal housing facilities to confirm procedures are being followed. Unanticipated adverse events (e.g., sickness and death) are documented and investigated by the researcher in consultation with animal attendants, welfare veterinarians and relayed to the committee; procedures are refined appropriately if the event is found to relate to experimental procedures. There are therefore an extensive set of integrated policies and personnel dedicated to animal welfare in biomedical research. This often exceeds the basic requirements of existing statewide regulation. Studies of regulatory compliance in animal ethics have concluded that the combination of external and internal ethics requirements has reached a point where additional regulations are unlikely to improve animal welfare with any efficiency⁵.

The highly regulated nature of animal research also means that work poses negligible risk for the people of NSW. For example, our research uses genetic techniques to study brain functions. However, these techniques can only be performed in specially certified PC2 facilities by researchers trained to work safely in these environments. The genetic tools we use are non-replicating, which means that they cannot infect a person and cause disease. Finally, all our biomedical waste is securely disposed of by a specialised medical waste contractor. As a result, animal research in NSW poses negligible risk. In fact, abolishing or restricting animal research would increase risks to the public because of how important animal research is as a risk reduction tool for the development of new medical technologies.

Three Ways to Improve Animal Welfare in NSW

Despite the importance of animal research, as well as the many steps and procedures already in place to care for the animals used in research, there are three significant ways that NSW could further improve the welfare of laboratory animals.

1. Support a local animal breeding facility

At present, there is no major supplier of animals for scientific research in NSW. Animals must be bred locally on site, which is not feasible in many facilities, or imported from interstate or overseas. In 2021, the Animal Resource Centre in Perth announced its closure despite being the largest supplier of

- Pritt, S., McNulty, J. A., Greene, M., Light, S., & Brown, M. (2016). Decreasing institutionally imposed regulatory burden for animal research. *Lab Animal*, 45(8), 297-300. <u>https://doi.org/10.1038/laban.1067</u>
- Thulin, J. D., Bradfield, J. F., Bergdall, V. K., Conour, L. A., Grady, A. W., Hickman, D. L., Norton, J. N., & Wallace, J. M. (2014). The cost of self-imposed regulatory burden in animal research. *The FASEB Journal*, 28(8), 3297-3300. <u>https://doi.org/10.1096/fj.14-254094</u>

⁵ Norton, J. N., Reynolds, R. P., Chan, C., Valdivia, R. H., & Staats, H. F. (2017). Assessing the satisfaction and burden within an academic animal care and use program. *The FASEB Journal*, *31*(9), 3913-3921. <u>https://doi.org/10.1096/fj.201700072RR</u>

laboratory animals in Australia⁶. However, even if ARC was not in the process of closing down, it is well known that transport is a major stressor for laboratory animals⁷.

If the NSW government is interested in improving the welfare of laboratory animals, supporting the construction and maintenance of a breeding facility in NSW must be a priority. Reducing transport stress is a viable method of significantly improving animal welfare through the 'refinement' strategy (one of the '3Rs'⁸) yet is mostly outside of the power of individual researchers to control. It therefore requires government intervention to ensure that researchers can source animals for essential animal experiments that are not subject to a 5-hour flight from Perth or even longer from overseas.

2. Provide targeted funding to upgrade animal housing in research institutions

A second way to improve animal welfare is to provide targeted funding to upgrade animal housing in research institutions. Laboratory rodents (i.e. rats and mice) are often kept in cages that do not allow them to express a full range of natural behaviours, such as burrowing or climbing. However, current standards of rodent housing evolved to prioritise economic considerations and ease of cleaning, largely at the expense of naturalistic behaviours⁸.

Upgrading animal facilities requires significant investment to purchase new cages, new racks, and equipment. It would also require an ongoing investment in additional animal care technicians and veterinary staff to maintain higher standards of care and clean more complex animal housing environments. In the absence of federal or philanthropic funding dedicated to improving animal welfare, it is impossible for individual researchers or research teams to implement these improvements. It is therefore necessary for government to provide targeted funding to refit current animal facilities to provide a standard of animal housing that provides more space and enrichment for laboratory animals.

3. Provide targeted funding to conduct research to improve animal welfare

Animal research does not only benefit humans but can also be used to benefit animals. Animal research projects might be aimed at conservation or at improving animal welfare in agriculture or in research laboratories. Many biomedical research scientists are passionate about animal welfare, conducting and publishing research identifying ways to improve research techniques⁹. However, funding of research to

⁶ Mallapaty 2021. Loss of Australia's largest lab animal supplier will leave 'huge gap'. *Nature News*. <u>https://doi.org/10.1038/d41586-021-01896-x</u>

⁷ Capdevila, S., Giral, M., Ruiz de la Torre, J. L., Russell, R. J., & Kramer, K. (2007). Acclimatization of rats after ground transportation to a new animal facility. *Laboratory Animals*, 41(2), 255-261. <u>https://doi.org/10.1258/002367707780378096</u>

⁸https://www.nc3rs.org.uk/

⁸ Makowska, I. J., & Weary, D. M. (2016). The importance of burrowing, climbing and standing upright for laboratory rats. *Royal Society Open Science*, 3(6), 160136. <u>https://doi.org/10.1098/rsos.160136</u>

⁹ Khoo, S. Y.-S., Lay, B. P. P., Joya, J., & McNally, G. P. (2018). Local anaesthetic refinement of pentobarbital euthanasia reduces abdominal writhing without affecting immunohistochemical

improve animal welfare is extremely scarce. Providing targeted grants to improve the welfare of animals used in biomedical research would enable and encourage biomedical researchers to spend more time developing refinements and alternatives to animal experimentation. Doing so should be a priority for funding agencies and researchers alike, since compromised animal welfare can undermine experimental integrity and reduce confidence in data, thus slowing scientific progress.

Conclusions

Animal research brings many benefits and carries negligible risk to society, which is perhaps why over three quarters of voters in Switzerland recently rejected a proposed ban on animal research in a February 2022 referendum¹⁰. Biomedical animal research is highly regulated and is an effective risk management strategy to protect human clinical trial participants and patients from experimental therapies that are unlikely to be safe or effective. New regulations in an already-highly regulated environment are unlikely to improve animal welfare. Instead, we suggest three approaches that would. A local breeding facility would significantly reduce stress associated with interstate or overseas freight. Funding to upgrade and operate animal facilities will enable animals to be housed in more spacious and complex environments that permit a wider range of natural behaviours. Finally, domestic funding dedicated to animal welfare will enable researchers to develop additional refinement strategies and alternatives to animal experimentation that can reduce or eliminate welfare impacts from biomedical research.

endpoints in rats. *Laboratory Animals*, 52(2), 152-162. https://doi.org/10.1177/0023677217721260

Khoo, S. Y. S., Correia, V., & Uhrig, A. (2020). Nesting material enrichment reduces severity of overgrooming-related self-injury in individually housed rats. *Laboratory Animals*, 54(6), 546-558. <u>https://doi.org/10.1177/0023677219894356</u>

¹⁰ https://www.reuters.com/world/europe/switzerland-vote-becoming-first-nation-ban-animal-testing-2022-02-13/