# [Review]
# Animal Experimentation: Working Towards a Paradigm Change. Edited by Kathrin Hermann and Kimberley Jayne. Brill, 2019. 714 pp.

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This is a very large volume. In almost 700 pages, no less than 51 authors contribute to 28 chapters (there is also a *Foreword*, by Peter Singer, and an *Afterword,* by John P. Gluck). The majority of chapters focus upon ethical or political matters and are readily accessible to scientists. Likewise, non-scientists ought to be able to follow the more technical or science-heavy chapters.

Taking their lead from recent European Union policy, specifically Directive 2010/63/EU, which prescribes the complete replacement of animals in research and education with non-animal alternatives 'as soon as it is scientifically possible' (xxiv), the editors, Kathrin Hermann and Kimberley Jayne, present a broad range of papers from a multidisciplinary group of authors. Be they lawyers, philosophers, veterinarians, scientists, or ex-animal researchers, the contributors all agree that there are fatal flaws in the existing animal experimentation paradigm.

The fatal flaw under scrutiny in Part Five of this volume is the animal model itself. The general point made in the eight papers is: whether the aim is to investigate disease or test the efficacy of drugs, you can't extrapolate findings from research on other animals to humans. As Ray Greek and Lisa Kramer put it, 'The failure of the animal model … is due to differences in gene response between humans and mice. Considering that humans and non-human animals are evolved species, there is no reason to expect other diseases or conditions would allow the animal model to have high predictive value' (405).

In addition to a historical survey of extrapolation failures, Greek and Kramer employ a theoretical device known as the Trans-Species Modelling Theory (TMT). The TMT incorporates insights from complex systems theory and evolutionary biology, as well as established research findings from animal model sceptics like Hugh Lafollette and Niall Shanks. The TMT states, 'While trans-species extrapolation is possible when perturbations concern lower levels of organization or when studying morphology and function at the gross level, one evolved complex system will not be of predictive value for another when the perturbation affects higher levels of organization' (393). In lay terms, it may be possible to extrapolate findings from animal research at one level, but it is not possible at the level of drug and disease research.

Like Greek and Kramer, Kathy Archibald, Robert Coleman and Tamara Drake also base their case against the animal model by appealing to empirical evidence. Drugs that were tested on animals with no ill-effects turn out to be toxic to humans; drugs that were ineffective on animals, like penicillin, were effective on humans (418-421). Archibald, Coleman and Drake also identify some purported flaws with clinical trials and, briefly, discuss some non-animal technological alternatives, such as an in-vitro micro-liver that can be used in hepatitis B research (426). (Parts Six and Eight of the volume provide a survey of animal-free alterative techniques in education and training (2 chapters), and product testing and basic research (5 chapters), respectively.)

In their contribution to Part Five, John J. Pippen, Sarah E. Cavanaugh and Francesca Pistolatto focus on the use of transgenic animals in Alzheimer's Disease (AD) research. (Genetically modified animals are also the focus of the following chapter by Jarrod Bailey.) Genetically modified animals are bred with brain pathologies similar to the pathologies found in deceased Alzheimer's patients. The medical orthodoxy is that Alzheimer's patients have plaque on their brains; the plaque causes inflammation and the inflammation, in turn, damages the neural networks and synapses, resulting in symptomatic behaviour. While they acknowledge that much of this research is successful, Pippen, Cavanaugh and Pistolatto claim that its predictive value is restricted to the particular species of transgenic animal concerned: '[T]hough various transgenic models develop specific phenotypical aspects of AD … no individual animal model or combination of models replicates the clinicopathological complexity of human Alzheimer or translates to improved outcomes for Alzheimer patients' (485). In other words,

the use of transgenic mice in AD research is telling us a lot about how certain drugs can relieve AD symptoms in genetically-modified mice but little about the efficacy of the drugs in human beings. Indeed, Pippen, Cavanaugh and Pistolatto present a table documenting 31 'notable' failed AD drug trials between 2013-2018 (489-490).

Ultimately, however, empirical evidence of a litany of drug trial failure bolsters the case for lowering our expectations about the usefulness of animal research. Such data suggests that we should be sceptical of bold claims about the efficacy and possible benefits of new wonder drugs. But a healthy scepticism towards animal research does not entail support for a paradigm change. The case for change also needs an ethical dimension, and the ethical case against animal research needs to make reference to distinctly ethical concepts (Arianna Ferrari stresses this point in her contribution (203)).

Parts Three and Four of the collection deal with ethics and politics. While none of the authors address the moral status of animals in a systematic way, they all more or less presuppose that animals matter enough to preclude them being used in research. Against the background of this framing assumption, the contributors present some original and engaging ideas. Jane Johnson and Anna Smajdor, for example, argue that people who conduct research on animals are morally injured in the process. The injury comes about as a consequence of a systemic process of reification: the 'diminution, denial or abrogation of moral agency' (311). The idea seems to be that treating animals like objects leads researchers to likewise view themselves as objects; cognitive dissonance, with accompanying feelings of disempowerment, purportedly ensues.

It is not clear, however, whether Johnson and Smajdor mean to suggest that the moral injury of reification is subjective, that is, necessarily tied to unpleasant feelings like dissonance and disempowerment, or objective, that is, injurious irrespective of how a researcher may feel. It is safe to say that there are many animal researchers who enjoy their work and feel it contributes to the meaningfulness of their lives. How are these researchers morally injured exactly? If the claim is that the injury of reification is subjective, then the scope of the critique is restricted only to researchers who feel bad about what they do. As a percentage of researchers overall, this may be a small number. Alternatively, if the claim is that the injury is objective, the charge of paternalism looms. It is paternalistic to claim that someone is *morally* injuring

themselves when they freely consent to participate in a contentious practice. Participation in animal research is no different in this respect to extra-marital sex, drug-taking, extreme sports and facial tattoos.

While Johnson and Smajdor aim to draw attention to the feelings of researchers, Mara-Daria Cojocaru and Philipp von Gall put the feelings of ethics committee members (and other regulatory experts) at the centre of their chapter. Moral doubt is the key emotion. Cojocaru and von Gall want the emotions of ethics committee members to inform regulatory deliberation and decision-making. Doubt, Cojocaru and von Gall argue, can serve two functions (299). Firstly, it can be an antidote to 'moral numbness' on the part of regulators; secondly, it can signal that there are too many question marks hanging over a particular research proposal. At such times, Cojocaru and von Gall suggest, '[T]he practice should not proceed, so that important opportunities to inquire into value conflicts are not missed' (299). In effect, for Cojocaru and von Gall, doubt functions like an alarm call that alerts regulators to fundamental problems with the research proposal under scrutiny. In line with Cojocaru and von Gall's view, when doubt arises, regulators should either defer a decision on the merits of a proposal to allow for further deliberation, or reject the proposal outright.

Improved regulation of research requires political will and political will, if the history of animal welfare regulation is any guide, tends to follow public outcry over the treatment of animals. If it is best to avoid knee-jerk policy responses made in the heat of controversy, then both sides of the animal research debate ought to approve of Monika Merkes and Rob Buttrose's call for greater transparency in animal research. On the one side, greater public scrutiny ought to motivate researchers to keep their house in order; on the other side, transparency would raise awareness of the nature and scale of research – an outcome proponents of animal rights should welcome. While their chapter focuses on the Australian scene, Merkes and Buttrose's proposals are relevant to any jurisdiction that operates in line with the existing paradigm. The proposals are: a public register of animal research license holders; the publication of layperson summaries of research proposals; the publication of the cost-benefit calculation sections of research proposals; the improved collection, and wider dissemination, of animal use data.

It is foreseeable that researchers would push back and argue that such proposals would expose them to the wrath of animal rights extremists. But, arguably, what's of more immediate

concern to animal researchers in the current political climate is social admonition. But a right to protection from ostracism by friends and family, when the contentious behaviour is the product of one's free choice to begin with, cannot be a basic right of anyone in liberal democracies, let alone anyone engaging in practices that operate under social license.

The most important condition of the social license for animal researchers is to do justice to the so-called Three-Rs of Animal Research. The Three Rs, reduction, refinement and replacement, are meant to function as normative principles for the design and conduct of animal research. First developed in the 1950s by William Russell and Rex Burch, the basic idea is that researchers have an obligation to *reduce* the number of animals they use, *refine* their procedures and, where possible, *replace* animals with non-animal alternatives. While laudable in theory, in practice, as a number of contributors to this volume point out, an almost exclusive focus on reduction and refinement has come at the expense of replacement. It is relatively easy for researchers to tweak their research proposals to satisfy the reduction and refinement conditions. Why request 500 mice, when you can use 300? Why euthanize a mouse with a painful intraperitoneal injection, when you can use an inhalation anaesthesia and then a guillotine? The replacement condition, on the other hand, is not so easy to satisfy. If the experimental aim is to learn about the impact of drugs on the cognitive function of mice, for example, then you need mice to ingest the drugs and perform the battery of behavioural tests. Replace the mice and the research does not proceed at all. Such an outcome would be unthinkable to most researchers, and explains why they don't take the replacement condition seriously. If there is one overarching theme of this volume, it is that replacement is the key to meaningful paradigm change.