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Adam Shriver

Editors

Neuroethics and Nonhuman Animals

Advances in Neuroethics

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Advances in neuroscience research are bringing to the forefront major benefits and ethical challenges for medicine and society. The ethical concerns related to patients with mental health and neurological conditions, as well as emerging social and philosophical problems created by advances in neuroscience, neurology and neurotechnology are addressed by a specialized and interdisciplinary field called neuroethics.

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L. Syd M Johnson • Andrew Fenton •
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Editors

Neuroethics and Nonhuman Animals

Springer

Editors
L. Syd M Johnson
Center for Bioethics and Humanities
SUNY Upstate Medical University
Syracuse, NY, USA

Humanities Department
Michigan Technological University
Houghton, MI, USA

Adam Shriver
Oxford Uehiro Centre for Practical Ethics
University of Oxford
Oxford, United Kingdom

Andrew Fenton
Department of Philosophy
Dalhousie University
Halifax, NS, Canada

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Editors and Contributors

About the Editors

L. Syd M Johnson is a philosopher/bioethicist/neuroethicist and Associate Professor in the Center for Bioethics and Humanities at Upstate Medical University. She is an Associate Editor for *Neuroethics* and a member of the NIH BRAIN Initiative Neuroethics Working Group. Dr. Johnson's books include *The Routledge Handbook of Neuroethics* (with Karen Rommelfanger, Routledge, 2018) and *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019), and her articles have appeared in numerous bioethics, neuroscientific, and medical journals. Her research focuses on ethical issues related to brain injuries, including sport-related neurotrauma, brain death, and disorders of consciousness, and her interest in all things with brains includes every kind of critter, zombies, and robots.

Andrew Fenton is Associate Professor in the Department of Philosophy at Dalhousie University. He has authored or coauthored papers related to animal philosophy or animal research ethics in such journals as *Biology and Philosophy*, *Cambridge Quarterly of Healthcare Ethics*, *Developing World Bioethics*, *Journal of Animal Ethics*, and *The Monist* and has chapters on these topics in *The Routledge Handbook of Neuroethics* (coedited by L. Syd M Johnson and Karen Rommelfanger, Routledge, 2018), *The Routledge Handbook of Philosophy of Animal Minds* (coedited by Kristin Andrews and Jacob Beck, Routledge, 2018), and the *Philosophy of Behavioral Biology* (coedited by Kathryn Plaisance and Thomas Reydon, Springer, 2012). Fenton has also been a part of a small but mighty group of philosophers submitting amici curiae in support of two cases spearheaded by the Nonhuman Rights Project. These recent efforts resulted in a coauthored book, *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019), whose royalties go to the Nonhuman Rights Project.

Adam Shriver is a Research Fellow at the Oxford Uehiro Centre for Practical Ethics and the Wellcome Centre for Ethics and Humanities at the University of Oxford. A graduate of the interdisciplinary Philosophy-Neuroscience-Psychology (PNP) program at Washington University in St. Louis, he has published articles at the intersection of animal ethics and the neurosciences in journals such as

Philosophical Psychology, *Neuroethics*, *The Cambridge Quarterly of Healthcare Ethics*, and *The Journal of Agricultural and Environmental Ethics*. Adam co-organized a pre-conference workshop on Animals and Neuroethics for the 2009 Society for Philosophy and Psychology annual meeting, coauthored the introduction to a special issue of the *Cambridge Quarterly of Healthcare Ethics* on Neuroethics and Animals (2014), and organized a 2016 workshop on Animal Research Neuroethics at the University of Pennsylvania with funding from the Alternatives Research Development Foundation.

About the Authors

Christophe Boesch is the director of the Department of Primatology of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. He is also the founder and president of the Wild Chimpanzee Foundation (www.wildchimps.org). Boesch's first field experience started in 1973, when he conducted census work on the mountain gorillas of Virunga National Park in Rwanda, under the supervision of Dian Fossey. In 1976, Boesch began his long-term fieldwork with chimpanzees at Taï National Park in Côte d'Ivoire. The Taï chimpanzee project has been ongoing since 1997 and includes students studying all aspects of the ecology, social organization, tool use, hunting, cooperation, food-sharing, intercommunity relationships, and cultural and cognitive capacities of this population of chimpanzees.

Culum Brown studies behavioral ecology of fishes with a special interest in cognition, personality, and laterality. He is Professor of vertebrate evolution at Macquarie University, coeditor of the volume *Fish Cognition and Behavior*, and Editor of the *Journal of Fish Biology*.

Tom Buller is Professor of Philosophy at Illinois State University. Recent publications include "The New Ethics of Neuroethics" (*Cambridge Quarterly of Healthcare Ethics*, 2018); "The Future of Neuroethics Research and Training" in *The Debate About Neuroethics,* edited by Racine E and Aspler J (Springer, 2017); "Advance Consent, Critical Interests, and Dementia Research" (*Journal of Medical Ethics*, 2015); and "Animal Minds and Neuroimaging: Bridging the Gap between Science and Ethics?" (*Cambridge Quarterly of Healthcare Ethics*, 2014).

Gary L. Comstock is Professor of Philosophy at North Carolina State University where he conducts research on ethical questions in the biological sciences. The author of two books, *Research Ethics: A Philosophical Guide to the Responsible Conduct of Research* (Cambridge University Press, 2013) and *Vexing Nature? On the Ethical Case Against Agricultural Biotechnology* (Kluwer, 2000), he is coauthor of *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019) and coeditor of *The Moral Rights of Animals* (Lexington Press, 2016). He has written on ethical

questions surrounding the study of animal behavior and neuroanatomy, the genetic modification of farm animals, the permissibility of hunting, machine medical ethics, and animal metacognition. Recent papers take up legal questions concerning the intrinsic value of companion animals and the merits of the argument for animal rights from overlapping species.

G. K. D. Crozier is Professor of Philosophy at Laurentian University in Sudbury, Canada, and cofounder of the multidisciplinary Centre for Evolutionary Ecology and Ethical Conservation. Dr. Crozier holds a Canada Research Chair in Environment, Culture and Values.

David DeGrazia is Elton Professor of Philosophy at George Washington University and Senior Research Fellow in the National Institutes of Health Department of Bioethics. His writings about animals include *Taking Animals Seriously: Mental Life and Moral Status* (Cambridge University Press, 1996), *Animal Rights: A Very Short Introduction* (Oxford University Press, 2002), and, with Tom Beauchamp, *Principles of Animal Research Ethics* (Oxford University Press, forthcoming 2019).

Rey Edison is a graduate student at the MIT Media Lab. Their current research includes considering genetic methods of improving animal well-being, modeling gene drives to assess safety and efficacy, and other technologies based on evolutionary principles.

Kevin Esvelt is Assistant Professor at the MIT Media Lab, where he leads the Sculpting Evolution Group in exploring evolutionary and ecological engineering. The first to realize that CRISPR "gene drive" systems could unilaterally alter wild populations of organisms, Esvelt and his colleagues revealed their findings and called for open discussion and safeguards before they demonstrated the technology in the laboratory. At MIT, the Sculpting Evolution Group develops localized technologies for community-guided environmental editing. Guided by the people of Nantucket and Martha's Vineyard, they are the technical hands of the "Mice Against Ticks" project aiming to prevent tick-borne disease and are working with Māori and other New Zealanders on humanely removing invasive rodents. Other research interests include unraveling the workings of molecular evolution and reducing animal suffering in the laboratory, the city, and the farm. An outspoken advocate of sharing research plans to accelerate discovery and improve research safety, Esvelt seeks to use gene drive as a catalyst to reform the scientific ecosystem. His work has appeared in major scientific journals, including *Nature* and *Science*, and features regularly in popular media, including *The New York Times*, *The New Yorker,* and *NPR*.

Andrew Fenton is Associate Professor in the Department of Philosophy at Dalhousie University. He has authored or coauthored papers related to animal philosophy or animal research ethics in such journals as *Biology and Philosophy*, *Cambridge Quarterly of Healthcare Ethics*, *Developing World Bioethics*, *Journal of*

Animal Ethics, and *The Monist* and has chapters on these topics in *The Routledge Handbook of Neuroethics* (coedited by L. Syd M Johnson and Karen Rommelfanger, Routledge, 2018), *The Routledge Handbook of Philosophy of Animal Minds* (coedited by Kristin Andrews and Jacob Beck, Routledge, 2018), and the *Philosophy of Behavioral Biology* (coedited by Kathryn Plaisance and Thomas Reydon, Springer, 2012). Fenton has also been a part of a small but mighty group of philosophers submitting amici curiae in support of two cases spearheaded by the Nonhuman Rights Project. These recent efforts resulted in a coauthored book, *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019), whose royalties go to the Nonhuman Rights Project.

Hope Ferdowsian MD, MPH, is a fellow of the American College of Physicians and the American College of Preventive Medicine. She has served as an assistant clinical professor of medicine at the George Washington University School of Medicine and Health Sciences, as an associate professor of Microbiology and Immunology at Georgetown University, and now as an associate professor in the Department of Internal Medicine at the University of New Mexico School of Medicine. As an internist and preventive medicine and public health physician, her expertise spans the fields of medicine, public health, and ethics. She has lectured in academic centers and public spaces in North America, Europe, Asia, Africa, and Australia. Internationally, she has worked in the Democratic Republic of Congo, Ethiopia, Kenya, Malawi, South Africa, Uganda, and the Federated States of Micronesia. Domestically, she works with nonprofit organizations providing healthcare and advocacy for vulnerable populations. Her work primarily focuses on the connections between the rights, health, and well-being of people and animals, and she has published broadly in this area. Her recent book, *Phoenix Zones: Where Strength Is Born and Resilience Lives* (The University of Chicago Press, 2018), also explores this topic.

Bob Fischer is Associate Professor in the Department of Philosophy at Texas State University. He is the author of *The Ethics of Eating Animals* (Routledge, 2019), *Animal Ethics—A Contemporary Introduction* (Routledge, forthcoming), and many essays on topics in applied ethics.

Simon Gadbois is the director of the Canid (and Reptile) Behaviour and Olfaction Laboratory in the Department of Psychology and Neuroscience at Dalhousie University. He integrates the disciplines of ethology, comparative psychology (animal psychophysics specifically), and neuroscience in his research, as well as the schools of zoosemiotics, post-cognitivism, and classical ethology. He worked closely with John Fentress, Peter McLeod, and Fred Harrington in lupine behavioral endocrinology and wild canid natural action sequences. He is a species generalist, having worked with invertebrates, fish, reptiles, birds, and mammals, and combines field work and lab experiments in his research. His current interests include reptile

conservation and the study of wild and domestic Canids, in particular social behavior, communication, and olfaction.

Robert Garner is Professor of Politics in the School of History, Politics and International Relations at the University of Leicester. He has published widely on animal ethics and politics. His books include *Animals, Politics and Morality* (Manchester University Press, 2004), *Animal Ethics* (Polity Press, 2005), *The Political Theory of Animal Rights* (Manchester University Press, 2005), and *A Theory of Justice for Animals* (Oxford University Press, 2013).

L. Syd M Johnson is a philosopher/bioethicist/neuroethicist and Associate Professor in the Center for Bioethics and Humanities at Upstate Medical University. She is an Associate Editor for *Neuroethics* and a member of the NIH BRAIN Initiative Neuroethics Working Group. Dr. Johnson's books include *The Routledge Handbook of Neuroethics* (with Karen Rommelfanger, Routledge, 2018) and *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019), and her articles have appeared in numerous bioethics, neuroscientific, and medical journals. Her research focuses on ethical issues related to brain injuries, including sport-related neurotrauma, brain death, and disorders of consciousness, and her interest in all things with brains includes every kind of critter, zombies, and robots.

Robert C. Jones is Associate Professor in the Department of Philosophy at California State University, Dominguez Hills. He works on questions at the intersection of applied ethics, animal cognition, speciesism, and social justice, with a focus on animal liberation theory and activism. He is a contributing author to *Chimpanzee Rights: The Philosophers' Brief* (Routledge, 2019), and his essays include "Animal Cognition and Moral Status" in *The Routledge Companion to Environmental Ethics*, edited by Andrew Light and Benjamin Hale (Routledge, forthcoming); "The Precautionary Principle: A Cautionary Note" (*Animal Sentience: An Interdisciplinary Journal on Animal Feeling*, 2017); "Veganism as an Aspiration" (with Lori Gruen) in *The Moral Complexities of Eating Meat*, edited by Ben Bramble and Bob Fischer (Oxford University Press, 2015); "Animal Rights is a Social Justice Issue" (*Contemporary Justice Review*, 2015); "Science, Sentience, and Animal Welfare" (*Biology & Philosophy*, 2013); and "A Review of the Institute of Medicine's Analysis of using Chimpanzees in Biomedical Research" (with Ray Greek, S*cience and Engineering Ethics*, 2014).

Lori Marino is a neuroscientist and expert in animal behavior and intelligence who was on the faculty of Emory University for twenty years. She is founder and president of *The Whale Sanctuary Project*, whose mission is to create the first permanent seaside sanctuary for captive orcas and beluga whales in North America. She is also executive director of *The Kimmela Center for Animal Advocacy,* a science-based nonprofit organization combining academic scholarship with animal advocacy. Dr. Marino has published over 130 peer-reviewed scientific papers, book chapters, and magazine articles on brain evolution, intelligence and self-awareness

in other animals, human–nonhuman animal relationships, and captivity issues, including "Self-recognition in the bottlenose dolphin: A case of cognitive convergence" (with Diana Reiss, *Proceedings of the National Academy of Sciences USA,* 2001); "Cortical complexity in cetacean brains" (with Patrick Hof and Rebecca Chanis, *The Anatomical Record*, 2005); "Brain structure and intelligence in cetaceans" in *Whales and Dolphins: culture, cognition and conservation*, edited by P Brakes, MP Simmonds, C Bass (Earthscan, 2011); "Do zoos and aquariums promote attitude change in visitors? A critical evaluation of the American Zoo and Aquarium study" (with Scott Lilienfeld, Randy Malamud, Nathan Nobis, and Ron Broglio, *Society and Animals*, 2010); and "Captivity" in *Critical Terms for Animal Studies*, edited by Lori Gruen (University of Chicago, 2018).

Letitia Meynell is Associate Professor of Philosophy (cross-appointed with Gender and Women's Studies) at Dalhousie University in Nova Scotia. Her work includes *Chimpanzee Rights: The Philosophers' Brief* (2019) with twelve coauthors, "Insight and Imagination: A New Account of the Content of Thought Experiments" (*Synthese*, 2014), and "Evolutionary Psychology, Ethology and Essentialism (Because What They Don't Know Can Hurt Us)" (*Hypatia,* 2012).

David M. Peña-Guzmán is Assistant Professor in Humanities and Liberal Studies at San Francisco State University. He holds an M.A. and Ph.D. in Philosophy from Emory University and has been a Postdoctoral Fellow at the Centre for Evolutionary Ecology and Ethical Conservation at Laurentian University and at the Berman Institute of Bioethics at Johns Hopkins University. His interests include animal studies, the history and philosophy of science, continental philosophy, meta-philosophy, and social theory. His work has appeared in journals such as *Animal Sentience, Foucault Studies, Hypatia,* and *Studies in History and Philosophy of Science Part A.*

Pandora Pound has been conducting research since 1990 and has worked within universities and medical schools throughout the UK, mainly in the field of public health. She was an early proponent of the need for systematic reviews of animal research and has published on the need for an evidence-based approach in this field. In 2017, she left academia to focus on this issue and to work toward more human-relevant approaches to the development and testing of medicines and now works for Safer Medicines Trust, UK. Her published papers include "Better science for safer medicines: the human imperative" (with K Archibald, K Tsaioun, and JG Kenna, *Journal of the Royal Society of Medicine,* 2018); "Is it possible to overcome issues of external validity in preclinical animal research? Why most animal models are bound to fail" (with M Ritskes-Hoitinga M, *Journal Translational Medicine* 2018); "Retrospective harm benefit analysis of pre-clinical animal research for six treatment interventions" (with CJ Nicol, *PLoS ONE* 2018); "Transparency and public involvement in animal research" (with R Blaug, *Alternatives to laboratory animals: ATLA*, 2016), 167–173; "Is animal research sufficiently evidence based to be a cornerstone of biomedical research?" (with M Bracken, *British Medical Journal*, 2014); and

"Where is the evidence that animal research benefits humans?" (with S Ebrahim, P Sandercock, M Bracken, and I Roberts, *British Medical Journal,* 2004).

Adam Shriver is a Research Fellow at the Oxford Uehiro Centre for Practical Ethics and the Wellcome Centre for Ethics and Humanities at the University of Oxford. A graduate of the interdisciplinary Philosophy-Neuroscience-Psychology (PNP) program at Washington University in St. Louis, he has published articles at the intersection of animal ethics and the neurosciences in journals such as *Philosophical Psychology*, *Neuroethics*, *The Cambridge Quarterly of Healthcare Ethics*, and *The Journal of Agricultural and Environmental Ethics.* Dr. Shriver co-organized a pre-conference workshop on Animals and Neuroethics for the 2009 Society for Philosophy and Psychology annual meeting, coauthored the introduction to a special issue of the *Cambridge Quarterly of Healthcare Ethics* on Neuroethics and Animals (2014), and organized a 2016 workshop on Animal Research Neuroethics at the University of Pennsylvania with funding from the Alternatives Research Development Foundation.

Lynne U. Sneddon Director, Bioveterinary Science, University of Liverpool, was the first researcher to discover nociceptors that detect painful stimuli in fish in 2002. Her empirical studies have driven the fish welfare agenda in many contexts and led to the development of a contemporary definition of animal pain. She is Chair of the Animal Section, Society for Experimental Biology; performs editorial roles for several journals; and is a research grant panel member for NC3Rs UK.

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Introduction to Animal Neuroethics: What and Why?

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L. Syd M Johnson

Abstract

The emergence and development of neuroethics over the last two decades has occurred in parallel with progress and advancement in several separate sciences, including various neurosciences, comparative psychology, comparative cognition, and ethology. The rapid growth of knowledge about animal brains, minds, intelligence, culture, behaviors, and capacities made by these sciences continues to be integrated into the philosophical discourse on animal ethics, but has thus far had little impact on animal research regulations. Our aim is to bend what have heretofore been more or less parallel tracks into convergence and intersection, and examine the implications of neuroscientific research for our understanding of the minds of other animals, the moral status of these animals, and our moral obligations to them. We challenge neuroethics to adopt a less anthropocentric focus and explore how growing knowledge of nonhuman minds challenges human supremacy.

1.1 Introduction

The emergence and development of neuroethics over the last two decades has occurred in parallel with progress and advancement in several separate sciences, including various neurosciences, comparative psychology, comparative cognition, and ethology. The rapid growth of knowledge about animal brains, minds,

L. S. M. Johnson (✉)

Center for Bioethics and Humanities, SUNY Upstate Medical University, Syracuse, NY, USA

Humanities Department, Michigan Technological University, Houghton, MI, USA
e-mail: johnsols@upstate.edu

intelligence, culture, behaviors, and capacities made by these sciences continues to be integrated into the philosophical discourse on animal ethics, but has thus far had little impact on animal research regulations. In this volume, our aim is to bend what have heretofore been more or less parallel tracks into convergence and intersection, and examine the implications of neuroscientific research for our understanding of the minds of other animals, the moral status of these animals, and our moral obligations to them. In so doing, we aim to challenge neuroethics to adopt a less anthropocentric focus and integrate new knowledge, a more inclusive ethics, and emerging scientific and technological innovations so as to expand its scope. So positioned, neuroethics can envision how a shift away from anthropocentrism could expand its role in critical discussions of our treatment of other animals and explore how growing knowledge of nonhuman minds challenges the human supremacy currently threatening our planet.

1.2   What Is Animal Neuroethics?

As this book demonstrates, some of the classic problems and concerns of neuroethics, such as cognitive enhancement, and the ethics of neuroscience and neuroscientific research, are reiterated in an animal-focused neuroethics. The traditional bifurcation of neuroethics, described by Adina Roskies as *the ethics of neuroscience* and *the neuroscience of ethics* [1], is certainly echoed in an animal-focused neuroethics. In the former category, the creation and use of nonhuman animals in neuroscientific research prompts questions that are obviously important to any animal-focused ethics, including neuroethics. A variety of animal species are used in neuroscientific and brain research, including basic research that seeks to map the brain, and understand brain cells and structures as well as their functions. Applied research uses a variety of animal models to understand diseases and disorders of the brain and mind, and to discover and test therapies. For example, some of the global big brain projects, like Japan Brain/MINDS, are currently focusing their efforts on the development and use of genetically modified nonhuman primates (NHPs), specifically marmosets.

Although the animal research industries as we know them began in earnest after the Second World War, research with animals and the use of animals as model organisms dates back centuries. To consider the ethical permissibility of using them in research challenges a well-entrenched scientific establishment built on the nearly unlimited use of animals [2]. Research ethics, at its best, is in the business of questioning and reevaluating the established use of certain (human) populations as research subjects, including children, and institutionalized populations such as prisoners and patients. An ethically and scientifically informed reevaluation of the use of animals cannot be beyond consideration simply because of the potentially enormous practical implications for the research enterprise. In a very real sense, this is an ethical problem that the behavioral and neurosciences have created—the success of the scientific study of animal brains and behavior in expanding our understanding of animal brains and minds, and the myriad ways that they are

structurally and functionally similar to human brains and minds, itself weakens longstanding scientific and ethical assumptions and presumptions about the permissible use of animals in neuroscientific research. In that way, an animal-focused neuroethics is both an *ethics of neuroscience* and a *neuroscience of ethics*—knowledge gained from the study of animal brains and minds can and must inform animal ethics.

While the use of animals in research has long been an important focus of animal ethics, research ethics, as well as the guidelines and regulations that govern research with animals, an animal-focused neuroethics must be more comprehensive and look beyond questions about the use of animal models in neuroscientific, cognitive, and psychological/psychiatric research. Just as a human-centered neuroethics is more than the ethics of brain research, an animal-focused neuroethics can look beyond research ethics. We anticipate that an animal-focused neuroethics will be uniquely positioned to push the boundaries of what neuroethics does and what issues it takes up. A number of novel concerns and themes emerged as this book took shape, pointing to the ways that an animal neuroethics is truly not just more of the same *with animals*, but rather something that promises to lead to an expansion of the scope of neuroethics. The diversity of the authors of the chapters in this collection also points to a promising expansion of the scientific disciplines that a more broadly focused neuroethics—already quite multi- and interdisciplinary—can and should welcome into the fold.

These novel (for neuroethics) themes, concerns, and disciplines include *comparative psychology* and *comparative cognition,* or research that compares the brains, minds, cognitive capacities, and behaviors of different species. Our focus in this book is primarily on what studies of animal behavior and cognition tell us about those animals, particularly with respect to whether they have the capacities commonly thought to confer moral status or moral concern. As noted below, however, viewing neuroethics in a less anthropocentric light will lead us to consider a variety of nonhuman entities, including those that are not biological organisms.

1.3   Animal Neuroethics: The What and the Why

In "Sentience and Consciousness as Bases for Attributing Interests and Moral Status: Considering the Evidence—and Speculating Slightly Beyond" [3], philosopher David DeGrazia begins with the assumption that sentient beings have interests and that having interests is sufficient (but perhaps not necessary) for moral status. He considers the state of the evidence for sentience in mammals and birds, reptiles, amphibians, fish, cephalopods, and arthropods (in particular, crustaceans and insects). In considering the possibility that insects are conscious but not sentient, DeGrazia goes farther afield and considers whether human-made robots might also one day be conscious but not sentient, eliciting implications for their moral status.

Philosopher Gary Comstock considers the cow in "Bovine Prospection, the Mesocorticolimbic Pathways, and Neuroethics: Is a Cow's Future Like Ours?" [4]. Like many farmed animals, cows get little respect and little recognition as

thinking, feeling creatures. Comstock considers the scant evidence for bovine cognition and asks what neuroscience can tell us, if anything, about the capacities of cows to think about the future. The question is important if having the right to a future—and a right not to be slaughtered—requires the ability to *think* about one's future. Comstock distinguishes several kinds of prospection and surveys what is known about the neuroanatomy of future-directed bovine beliefs and desires to ask whether a cow's prospection is *like ours*, where that is understood to include *all* human beings.

If cows get little respect, fish get even less, and their mental lives are quite poorly understood. In "Mental Capacities of Fishes," fish researchers Lynne Sneddon and Culum Brown [5] review the evidence for sentience and cognitive abilities in fishes to highlight the growing empirical evidence of their mental capacities. The evidence for pain, and for the capacities to experience positive and negative welfare states such as fear and stress, are still debated when it comes to fishes. Fish models are increasingly used in a wide variety of experimental contexts and their adoption is growing globally, although they are too frequently excluded from animal welfare regulations. But if fish are sentient and can suffer, this has ethical implications for their use in scientific studies and for current regulatory schemes that exclude them from welfare considerations.

In his chapter "The Four Cs of Modern (Neuro)ethology and Neuroethics: Cognition, Complexity, Conation and Culture," canid neuroethologist and neuroendocrinologist Simon Gadbois [6] critically engages what he sees as the *over-use* of certain kinds of mental state ascriptions to explain or model animal behavior. Though Gadbois rejects the traditional Behaviorism and early Ethology that each shunned the use of mentalistic terms in their scientific analyses of animal behavior, he reminds us that what looks to be quite complex behavior can arise from very simple psychological mechanisms or neurological processes. What's more, for Gadbois, much behavior need not reflect complex or *any* mental representations beyond that which permits an animal, based on past experience, to see what uses objects or individuals in their environment afford them and to be moved to behave accordingly. Rather than emphasizing cognition, Gadbois suggests a return to explanations that either do not require the ascription of mental states or foreground the role of emotions, innate motivations, and preferences.

In "Speciesism and Human Supremacy in Animal Neuroscience," philosopher Robert C. Jones [7] contends that the kinds of scientific and philosophical arguments used to deny the moral considerability of nonhumans reflect a kind of anthropodenial embedded in speciesism and, specifically, human supremacy and neurotypicalism. Skepticism regarding animal minds, cognition, and experience (e.g., reluctance to attribute thoughts, beliefs, phenomenal consciousness, and sentience) is frequently justified by reference to what we might call physiological heterologies in neural structure as well as differences in cognitive complexity when comparing humans and other animals. Underlying such claims are nonscientific, normative assumptions about human supremacy. Jones argues both that there is good reason to believe that vertebrates such as fish—and even invertebrates such as some crustaceans,

insects, and arachnids—are experiencing beings and that these conclusions have ethical implications.

Another theme that emerged in a substantive and interesting way in the book is *captivity*. The ethics of using captive populations in research has long been a concern of research ethics, given the dark history of exploiting vulnerable, easily accessible, captive populations like institutionalized children and incarcerated persons. Captivity for animals used in research, and the way it affects both the quality of life of the animals and the quality of the science [8], is an important issue for both neuroscience and neuroethics. The effects of captivity and social deprivation on both animal welfare and the ecological validity of cognitive and brain research are important considerations that bear on the value of such scientific research with animals [9–11]. Other captive animals—those in zoos and aquaria, for example—have not been a traditional concern for neuroethics. Several chapters look at the psychosocial, neurological/neurodevelopmental, and health effects of captivity on animals, as well as the deleterious effects of captivity on the quality and value of research.

In "The Human Challenge in Understanding Animal Cognition," primatologist Christophe Boesch [12] critically examines the emphasis on controlled experiments with captive animals in comparative cognition studies. Animals raised in captivity and living in laboratories, he argues, are completely detached from species-typical socio-ecologies, and studies of captive animals limit the progress of science. While studying free-living animals in their native environments—like the chimpanzees Boesch studies—has provided a wealth of detailed observations on sophisticated cognitive achievements, captive experimental studies have for too long concentrated on the "failure" of nonhuman species to demonstrate so-called uniquely human cognitive skills. If we want to understand the evolution of human and human-like cognitive abilities, Boesch argues that we must integrate information about brain plasticity and consider ecological validity and population differences.

In "Large Brains in Small Tanks: Intelligence and Social Complexity as an Ethical Issue for Captive Dolphins and Whales," neuroscientist Lori Marino [13] examines the effects of captivity on cetaceans, who are highly complex, large-brained social mammals. While dolphins have been used in research and for military purposes, the primary reason dolphins and whales are kept in captivity is for entertainment—thousands are kept in concrete tanks in marine parks and aquaria around the world. In these environments, these animals experience a lack of control, a lack of stimulation, a diminished social world, and the loss of the ability to engage in activities necessary for them to thrive. That they are such complex, self-aware, intelligent beings makes it more difficult for them to cope with artificial environments, Marino argues, resulting in stereotypies, self-harm, reduced life expectancy, and negative short- and long-term health effects. Marino thus establishes that traditional concerns of the animal rights and animal welfare communities—animal captivity and exploitation for entertainment—are also neuroethical concerns insofar as it is the effects of captivity on the cognitive capacities and psychological lives of cetaceans that amplifies the harm experienced by these social creatures. Marino concludes that the only ethical response is to phase

out the captivity of dolphins and whales for entertainment and move those in commercial facilities to sanctuaries that can better meet their needs.

Political philosopher Robert Garner explores what animal ethics has to say about the issue of captivity in "Animal Rights and Captivity in a Non-Ideal World" [14]. The best-known theories of animal rights are prohibitionist and/or abolitionist when it comes to using animals and keeping them captive. This would, of course, have significant implications for human use of and interactions with animals, including in science. One response is to reject animal rights in favor of welfarism, which permits use and captivity within limits related to animal welfare. Garner considers whether a more nuanced, interest-based rights theory would allow the claim that at least some animals do not have a strong enough interest in liberty to be accorded a *right* not to be kept in captivity. Another approach would involve the adoption of a non-ideal theory of animal rights, which would bracket liberty—and the issue of captivity—as a component of an ideal theory and therefore not of immediate ethical concern.

The position of animals within society, as well as within science, is mirrored, for better or worse, in certain human populations as well. The psychosocial and neurological/neurodevelopmental effects of captivity on *humans* are a concern for neuroethics to take up in a way that is informed by the brain sciences and driven by important sociopolitical considerations [15]. It's an area where neuroethicists—as philosophers, legal scholars, social scientists, neuroscientists, and animal scientists—can actively participate in a critically important public discourse as human mass incarceration and the use of solitary confinement become the focus of social and political attention and activism [2]. Studying the effects of captivity on animals in a way that is attentive to how captivity itself frustrates the fulfillment of important needs, alters behavior, and alters the brain and mind can inform our ethical, social, and legal thinking about the ethics of human captivity. What we learn about captivity in humans can also inform the way we view the captivity of nonhuman animals in the various settings in which they are kept. This is especially true of the large, social mammals most like us, including many NHPs used in research and for entertainment, and the elephants and cetaceans held in zoos and aquaria.

Animals used in *agriculture*, and neuroethical questions related to agriculture and agricultural research, are themes present in several chapters of this book, which consider the numerous species that are farmed, captured, and killed for food. Agriculture and the agricultural sciences have never been a part of neuroethics as it has heretofore been framed, and this new avenue promises interesting and fruitful intersections with the ascendant field of food ethics.

The aforementioned chapters on cows and fishes consider the cognitive capacities of species traditionally farmed and killed for food. Chapters by Edison and Esvelt, and Fischer, consider a traditional neuroethics question—enhancement—in the context of agricultural animals. Both chapters consider how animals might be genetically altered to enhance their welfare within intensive farming environments—genetic versions of what Bernard Rollin has referred to as *technological sanders*. "Under industrial conditions . . . animals do not naturally fit in the

niche or environment in which they are kept, and are subjected to 'technological sanders' that allow for producers to force square pegs into round holes—antibiotics, feed additives, hormones, air handling systems—so the animals do not die and produce more and more kilograms of meat or milk" (p. 106 in [16]). Edison and Esvelt, and Fischer, examine using genetic modifications not to enhance productivity per se, but rather to reduce animal suffering as those square pegs are forced into round holes.

In "On Mitigating the Cruelty of Natural Selection Through Humane Genome Editing," gene drive researchers Rey Edison and Kevin M. Esvelt [17] consider the possibility that future insights into the genetics of mood will enable us to substantially improve the lives of trillions of agricultural animals. Breeding and artificial selection already govern the genetics of billions of domesticated animals, as well as their predisposition to well-being. Edison and Esvelt outline the moral responsibilities of those who choose to engage with the problem of enhancing the welfare of farmed animals and discuss possible approaches for evaluating the efficacy of genetic methods. They address the concern that over-optimizing for indirect measures of well-being may reduce the extent to which we can be confident that those phenotypes are still meaningful indicators of what we are trying to measure. Given that animals used in agriculture are already selectively bred, what are the implications of using genetic methods to improve animal well-being in intensive farming environments?

Philosopher Bob Fischer takes up that question as well in his chapter "In Defense of Neural Disenhancement to Promote Animal Welfare" [18]. Fischer argues that animal welfare advocates don't act wrongly if they promote research into ways of neurally disenhancing animals. Whereas neuroethics has traditionally considered the implications of neural or cognitive *enhancement* in humans, Fischer focuses on *disenhancement* and contends that, while it may be a less than ideal solution to welfare concerns related to agricultural animals, it has the potential to reduce a tremendous amount of suffering. Disenhancement is not as bad, morally speaking, as it can initially seem to be, Fischer contends, and is a promising way of mitigating the suffering of animals who live in confinement in intensive agricultural operations.

Neuroethical concerns about the creation of chimeras—particularly mice with human brain cells—have frequently focused on the possible "humanization" of these creatures, with ethical implications for their welfare and use in research. That is, one of the concerns about research that creates chimeric animals is that the research itself might result in animals that it would be wrong to use in research because they could develop human-like intelligence or other capacities that might enhance their moral status. In "Nonhuman, All Too Human: Towards Developing Policies for Ethical Chimera Research," philosophers G.K.D. Crozier, Andrew Fenton, Letitia Meynell, and David M. Peña-Guzmán [19] address the ethical challenges raised by chimera research policy, using as a case study the National Institutes of Health proposal to change its policy governing the funding of human-nonhuman animal chimera research. The authors find a troubling shift from a focus on nonhuman animal *welfare* to poorly thought-out concerns with *humanization*. They raise concerns about modifying animals in ways that could significantly impact neurological

functions and behavioral capacities, with serious implications for the welfare of research subjects. The authors endorse robust restrictions on chimera research, particularly in the face of a growing globalization of research in varied and inconsistent regulatory environments, and argue that policies should not be based on beliefs about inherent human uniqueness. Instead, at a minimum, they should conform to the widely accepted 3Rs framework for research involving nonhuman animals, our best welfare science, and our best understanding of the capacities of other animals, unspoiled by a denial of relevant similarities.

In many societies it is commonplace to save or spare some animals at the expense of others, and to make judgments accordingly in ways that would be unconscionable were the relevant individuals humans. Philosopher Adam Shriver's chapter "The Role of Neuroscience in Precise, Precautionary, and Probabilistic Accounts of Sentience" [20] indirectly engages policy and applied ethical discussions that touch on anything from animal rescues in disaster zones to the use of animals in science. Shriver's chapter provides a critical discussion of minimizing harms to animals in the face of uncertainty about which animals are sentient. He examines three possible accounts that purport to guide decisions to that end: precise, precautionary, and probabilistic accounts of sentience. One challenge faced by policymakers and ethicists in the domain of animal welfare is that there is little consensus about what constitutes *good* evidence for sentience and how research from the neurosciences might add to evidence of sentience. Where it's possible to save or spare many animals, and erring on the side of assuming sentience is not overly costly, Shriver suggests that applying the Precautionary Principle—taking precautionary measures when sentience is not scientifically confirmed—is the right approach. The implication is that neuroanatomical similarities—and confirmatory neuroscientific evidence—may sometimes *not* be required where there are concerns about animal life or welfare. Many other cases, however, would require a weighting principle that incorporates an assessment of the likelihood of sentience into decisions about use or intervention. Precise accounts of sentience, Shriver argues, are not directly relevant for ethical decision-making, but nevertheless must be pursued in order to better refine the other accounts.

The final section of the book looks at questions about the *ethics of neuroscience* and specifically the use of animals in brain research. These chapters variously explore how research regulations can respond to the global increase in the use of nonhuman primates (NHPs) in a way that aligns with moral concerns about these animals, how a scientifically informed and enhanced understanding of animal welfare and well-being can refocus animal research ethics, and how brain research on animals has frequently failed to deliver benefits for humans—the very benefits used to justify harmful, invasive research.

In "A Threshold Standard for Regulating Invasive Nonhuman Primate Research in the Age of the Major Brain Projects," philosopher Tom Buller [21] examines animal welfare regulations in several countries that are currently ramping up their use of NHPs in brain research. Concern about the use of NHPs—who have complex social and environmental needs that are impossible to replicate in captive, laboratory settings—has increased as more is understood about these animals. At the same time,

the genetic modification of NHPs, and their development as models of human brain disorders, is a significant part of some of the national big brain projects, especially in Japan, China, and the United States. There is considerable variety in the national and international regulations governing the use of these animals. Buller examines these regulations and argues that in order for the various national projects to gain broad public support *and* provide adequate protection for NHPs, it is important that the regulations are harmonized and set an appropriate balance between protecting animals while encouraging scientific investigation and progress. Buller considers a number of approaches to tightening the regulations and concludes that the most satisfactory approach is to adopt a threshold standard of invasiveness.

Physician and human and animal rights advocate Hope Ferdowsian, in "The Right to Bodily Sovereignty and Its Importance to Mental and Physical Well-being" [22], describes how respect for bodily liberty and integrity (or bodily sovereignty) have driven the creation and enforcement of relevant rules and regulations in human subjects research, as reflected in documents like the Belmont Report. Little to no attention, however, is given to respect for the bodily sovereignty of nonhuman animals in research or other areas of society, despite its importance in determining health and well-being. As our understanding of well-being and the welfare needs of all animals grows, a more nuanced view of autonomy and vulnerability in both human and nonhuman animals is called for. Freedom from bodily trespasses and freedom of choice are critical to health and well-being in both human and nonhuman animals, and Ferdowsian argues that rules and regulations governing the protection of nonhuman animals should be updated to reflect our scientific understanding of these needs.

Philosopher and neuroethicist L. Syd M Johnson's chapter "The Trouble with Animal Models in Brain Research" [23] focuses on two problems with animal models used in neuroscientific research: the failure of many animal models to yield useful and beneficial information, and the ethical dilemma built in to claims about the similarity-based usefulness of an animal model, which is especially acute in the context of brain-related research. The chapter uses as a case study the well-known and well-studied failure of animal models in stroke research. The ethical dilemma arises because the similarity of the animals to humans is part of the scientific justification for using them—but their similarity to humans is also a reason to acknowledge their moral considerability. Indeed, as we learn more about animal minds and brains through neuroscientific research, as well as psychological, ethological, and comparative psychology research, the problem becomes only more acute. The successes of these sciences are themselves working to undermine the justification for further use of animals in research.

The essentially Utilitarian cost/benefit claim that human benefits justify harms to animals in research is undermined if those benefits consistently fail to materialize. Matters are even more serious if there is the potential for significant harm to humans, including opportunity costs, wasted resources, and risks to human research subjects. Considering the costs, harms, and benefits of animal research is foundational to regulatory approvals of animal research and the basis of animal research ethics as it is currently practiced within the scientific and regulatory community. But the

balance of harms and benefits is heavily tipped to favor human interests. An honest reckoning of the costs and harms to animals *and* the purported benefits to humans is unlikely to support the *status quo* because very little research will be useful or needed, and thus very little will be ethically justifiable.

Medical sociologist Pandora Pound examines the impact of preclinical animal research on the treatment of human traumatic brain injury in "Animal Models and the Search for Drug Treatments for Traumatic Brain Injury" [24]. Pound describes several scientific problems with the use of animal models, including poor internal and external validity, the difficulty of replicating human pathophysiology, and the near impossibility of recapitulating the human clinical context in animals. She argues that the evidence suggests that animal research into traumatic brain injuries is crude, harmful, and ineffective. Pound concludes that it's highly unlikely that modifications to preclinical studies can solve these problems and that animal models will never be fully scientifically valid, no matter how many improvements or modifications are attempted. Like Johnson, Pound argues that the Utilitarian harm/benefit calculus that provides the dominant ethical framework for justifying research with animals is undermined when the shortcomings of animal research, and the failure to yield benefits for humans, are accurately calculated.

1.4   Concluding Thoughts

The refocusing toward a less anthropocentric neuroethics is already beginning, as neuroethicists have considered the ethical questions raised by the development of engineered organisms, engineered neural circuitry, and the possibility of sentient machines. These organisms include neural organoids (also called cerebral organoids, or "mini-brains"). These small clusters of cultured, in vitro brain cells are important models for studying brain function, development, and brain disorders. As more complex organoids [25] and networks of organoids that could link different cell types—more closely approximating the functions of a whole brain—are created, urgent questions arise about the ontological and moral status of these organisms, as well as the philosophical implications of the existence of living, extracorporeal brain-like and brain-origin organisms. Ex vivo human brain tissue can currently be maintained in culture for months, perhaps even years. In 2019, researchers at Yale announced that they were able to restore circulation, cellular and electrical function, and perfusion in pig brains taken from slaughtered animals that had been dead for several hours [26]. Human-animal chimeras are engineered for a number of purposes, including for use as models of human disorders. The ethical implications of creating human-like characteristics in mice with human neuron cells have been among the neuroethical issues such research has raised [27], but as human-NHP chimeras are created, such concerns promise to be resurrected. Neuromorphic computing can simulate and investigate dynamic neural processes and identify more efficient approaches for computing [2, 28]. As these machines become more complex, the possible emergence of properties like self-awareness could challenge longstanding assumptions that only biological systems—specifically humans—can

possess such characteristics, and that only biological organisms warrant moral consideration.

All of these entities, whether they are human-engineered, of human origin, or of animal origin, are of neuroethical interest because of the unique philosophical, social, and cultural status of the brain and mind as the locus of personhood, rights, and moral status. As an interdisciplinary field, neuroethics is positioned to interrogate longstanding scientific and ethical assumptions about the special significance of humans and humanity. Neuroethics has established itself as a discipline that is forward-looking—sometimes to a fault as speculative outcomes and consequences of neurotechnologies fail to materialize. But looking and thinking ahead, and carefully, about the creation and instrumentalization of neural, neural-origin, and neural-inspired entities must be part of the remit of a forward-looking neuroethics.

And a neuroethics that looks beyond straightforwardly human entities must necessarily include nonhuman animals. There is a diverse, deep, and rich body of philosophical literature on animal ethics, but a specifically "animal neuroethics" has yet to emerge, although there have been efforts to connect the two [29]. Our aim, in this book, is to introduce the questions, concerns, and challenges of an animal-focused neuroethics and to point the way forward to a neuroethics that is altogether less anthropocentric. Such a neuroethics will be pushed as a field to move beyond some of its traditional concerns and questions. It will be better positioned to tackle both the novel and familiar problems, and engage with the intriguing puzzles and possibilities that will arise as more and more nonhuman, near-human, and human-created organisms and entities emerge as the brain sciences advance. At the same time, some of the essential issues and questions of an animal-focused neuroethics will also inform and expand our thinking about new directions and concerns regarding humans and human-centered neuroethics.

Finally, our understanding of animals and what makes them matter (or not) will help shape and inform our understanding and thinking about other near-human and human-origin organisms and entities, including neural organoids, synthetic embryos, human-animal chimeras, robots, and artificial intelligence. In the best case, it may clarify our thinking about those entities, but there is also the possibility—one neuroethics should be prepared to grapple with—that it will further *complicate* our thinking about them.

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