INTERNATIONAL JOURNAL OF COMPARATIVE PSYCHOLOGY

2018, 31
David Washburn
Special Issue Editor
Peer-reviewed

The Value of Duane Rumbaugh's Comparative Perspective—in Neurobiology

John Bickle

Departments of Philosophy and Psychology, Institute for Imaging and Analytical Technologies (I²AT), Mississippi State University;
Department of Neurobiology and Anatomical Sciences, University of Mississippi Medical Center

One commonality across the wide-ranging influences that Duane Rumbaugh had on late 20th century science was his commitment to the comparative perspective in psychology. I argue here that a commitment similar in force to Rumbaugh's also infuses mainstream experimental neurobiology. This connection is ironic because Rumbaugh eschewed brain intervention experimentation in vivo throughout his scientific career. Still, the influence and value of a perspective similar to Rumbaugh's can be found in neurobiology in at least three places. First, recent neurobiology has made good on one of Rumbaugh's predictions, that rearing and early environment will be shown to influence behavior and cognition in nonprimate animals. Second, the epistemologically justified use of animal models in experimental neurobiology to investigate human brain mechanism presupposes a strong commitment to the comparative perspective. Third, commitment to the comparative perspective raises the most pressing ethical concern in neurobiology: Namely, how is it ethical to perform brain intervention experiments on animal models if their brain mechanisms and behaviors compare closely enough with ours to justifiably generalize these experiments' results?

Keywords: comparative perspective, rearing and early development, animal models in neurobiology, ethics of in vivo experiments

As evidenced by the papers in this collection (as if this needed evidencing), the scope of Duane Rumbaugh's scientific contributions and influence was vast. I want to explore one topic that Rumbaugh did not discuss much, although it was central to his scientific work throughout his long, illustrious career. That topic is Rumbaugh's commitment to the comparative perspective in psychology, and the value of that perspective to the discipline. I suppose that Rumbaugh did not feel the need to elaborate explicitly on this topic, since his scientific results spoke directly for it. But it is useful to explore its specifics, because a comparative perspective similar in strength and content to Rumbaugh's also informs other sciences. One of these other sciences, ironically, is laboratory neurobiology.

I say "ironically" because the name "Duane Rumbaugh" and the term "laboratory neurobiology" rarely occur together. Rumbaugh and his primatologist collaborators sometimes used neural terms and concepts in their writings: Prefrontal cortex, brain complexity (Rumbaugh, 1997; Rumbaugh, King, Washburn, Beran, & Gould, 2007).[1] But so used, these were terms of gross functional anatomy. They signified activity and structures in primate brain regions related to stimulus salience, ecological niches, and adaptive learning beyond simple associations. Rumbaugh's interest in the brain was not in the realm of experimental laboratory neurobiology. His disinterest appears to be due to laboratory neurobiology's central use of invasive brain interventions within in vivo experiments, especially in mammals, as a method in the field's question to discover neuronal mechanisms generating cognition and behavior. Rumbaugh exhibited no professional interest in these

[1] I thank an anonymous reviewer for calling my attention to these two essays of Rumbaugh's.

Please send correspondence to John Bickle, Departments of Philosophy and Psychology, and Institute for Imaging and Analytical Technologies (I²AT), Mississippi State University; Department of Neurobiology and Anatomical Sciences, University of Mississippi Medical Center (Email: jb1681@msstate.edu) https://doi.org/10.46867/ijcp.2018.31.03.01

experiments or this goal. There is some evidence to suggest that he found such experiments deeply ethically problematic. Despite his personal disinterest in the field, however, I will argue here that contemporary laboratory neurobiology shares a commitment to the strength and the value of the comparative perspective very similar to Rumbaugh's commitment. This shared commitment can be found in three aspects of contemporary laboratory neurobiology:

1. Recent laboratory neurobiology has found early rearing and developmental influences on cognition and sociality in other mammals. Such influences and effects in primate cognition were central to one of Rumbaugh's few explicit arguments for the value of the comparative perspective in psychology. In fact, Rumbaugh predicted in print that such influences would be found in nonprimate animals, although of course the specificity of the recently discovered neurobiological mechanisms of these effects would have astounded him.
2. The specific ways that laboratory neurobiological experiments employ animal models and the practices by which their results are justifiably extended to human brains and cognition require a strong commitment to a comparative perspective much like Rumbaugh's.
3. This strong comparative perspective in turn generates the ethical concern of using these animals in intervention experiments, especially in brain intervention experiments, since the comparisons here are with the very features we take to give us human ethical status. The strength of the comparative perspective in laboratory neurobiology is reflected in the widespread recognition of this most pressing ethical concern. It is one that every neurobiological experimentalist who works with animal models confronts and ultimately must reconcile to his or her own satisfaction.

I address each of these illustrations of the comparative perspective in laboratory neurobiology in separate sections below.

Comparable Influences on Cognition, From Primates to Rodents

I start with one of Rumbaugh's and collaborators' few scientific publications that addressed explicitly and head-on the value of the comparative perspective in psychology (Rumbaugh, Savage-Rumbaugh, & Washburn, 1996). Their topic in this essay was the lessons of primate research discoveries as of the late 20th century. Their broadest intellectual target was Rene Descartes' much discussed (many nowadays would label it infamous) conception of nonhuman animals as "soulless" and thereby mindless mechanical automata. One often quoted passage on this topic from Descartes' corpus appeared in his *Discourse on the Method*:

> For after the error of those who deny God … there is none that leads week minds further from the straight path of virtue than that of imagining that the souls of beasts are of the same nature as our own. (1637/1988, p. 46)

(However, some Descartes scholars take issue with this standard reading of Descartes on animal minds [see, e.g., Cottingham, 1978].)

In response, Rumbaugh et al. (1996) titled an early section of their paper "Rejection of the 'beast-machine'." They claimed that this very rejection of the standard Cartesian conception of animal minds (or lack thereof) was what enabled recent primatologists to make their comparative discoveries: "Behavioral primatologists have made revolutionary advances because they have eschewed the 'empty organism' or

'empty box' perspective" (Rumbaugh et al., 1996, p. 115). Charles Darwin instead is the group's intellectual hero:

> Behavioral primatologists have reason to proceed with confidence that Darwin was correct in his postulation of *psychological* as well as biological continuities between animals and humans. Accordingly, if there is a compelling reason for us to accept the value of a process or construct for understanding human behavior, we should not rule out the possibility that traces thereof can be discerned at the nonhuman level. (Rumbaugh et al., 1996, p. 123)

They noted one especially pertinent comparative psychological factor across nonhuman to human primates, early rearing and environment as paramount for normal cognitive and social development: "Primates are, in measure, reflections of their early rearing and environments, and that early environment is crucial to the development of normal, socially competent primates" (Rumbaugh et al., 1996, p. 115). Nor did Rumbaugh and collaborators think that this comparative perspective ends with nonhuman primates:

> The future will likely reveal that much of the perspective advanced herein for primates holds in measure, for many other forms of life as well. One certainly must be intrigued by that possibility, given all that behavioral primatologists have learned …" (Rumbaugh et al., 1996, p. 123)

This comparative emphasis on early environment and rearing is certainly not original or unique to Rumbaugh and colleagues. Previous comparative psychologists had it (Harlow, Hebb), as well as psychologists in other traditions (Watson, Skinner). But Rumbaugh and colleagues explicit connection of early environment and rearing to the value of the comparative perspective takes us immediately to the recent work of neurobiologist Michael Meaney and colleagues and their rodent model of epigenetic programming of offspring stress responses by maternal nursing behaviors. The lab's most-cited paper (Weaver et al., 2004; 5,193 citations in PubMedCentral as of 8/16/2018) extended previously established results investigating rat maternal nursing styles on offspring fear and stress responses into adulthood. Rat offspring whose mothers licked and groomed them extensively (high-LG) and engaged in an arched-back nursing posture (high-ABN) showed greatly diminished bloodstream corticosterone levels and attenuated behavioral responses in restraint and forced swim tests compared to offspring of low-LG and -ABN mothers. The former is a common physiological measure of, and the latter are common rodent behavioral protocols for, reduced stress and fear responses. These differences had already been shown to persist into offspring adulthood, well past the weaning period. They are also susceptible to cross-fostering. Offspring of high-LG/ABN mothers cross-fostered to low-LG/ABN mothers displayed the physiological and behavioral stress and fear responses of non-cross-fostered low-LG/ABN offspring, and vice versa. Weaver et al.'s (2004) and Weaver et al.'s (2005) ingenious intervention experiments demonstrated a mechanism for this epigenetic maternal programming. They found differential methylation patterns at key sites on the promoter region of an offspring hippocampus glucocorticoid receptor gene; specifically, at sites producing differential subsequent effects on that gene's transcription and translation. These molecular-genetic differences in turn generated differential activities at this crucial entry point into the mammalian hypothalamic-pituitary-adrenal (HPA) stress axis. Working with neurobiologist Moshe Szyf, Meaney's lab was able to intervene directly into these DNA methylation patterns at these key sites and directly alter offspring physiological and behavioral stress and fear responses. Subsequent work from Meaney's lab established similar methylation patterns on a promoter site of the human homologue hippocampus glucocorticoid receptor gene. These patterns depended on early childhood traumatic experiences, and the high methylation patterns were found in young adult suicide completers compared to non-suicidal age-matched

controls. (For those interested in an overview of the experimental details of these studies, see Bickle and Kostko [2018]. Their presentation is explicitly for non-molecular neurobiologists.)

These scientists' own descriptions of their results are illuminating for my point in this section. After their initial cross-fostering, gene methylation, and intervention experiments, Weaver et al. wrote that "our findings provide the first evidence that maternal behavior produces stable alteration in DNA methylation and chromatin structure, providing a mechanism for the long-term effects of maternal care on gene expression in the offspring" (2004, p. 852). After intervening directly to increase methylation at these key gene sites and generating low-LG/ABN responses in high-LG/ABN-raised pups, they wrote: "The epigenetic mechanisms mediating this maternal behavior caused through gene expression generate the lifespan effects in offspring. Maternal LG-ABN behavior thus constitutes environmental programming of adaptive stress responses across generations" (Weaver et al., 2005, p. 11045). And after establishing similar methylation patterns in the human hippocampus glucocorticoid receptor gene homologue in a (extreme!) human measure of behavioral stress, McGowan et al. (2009) wrote:

> Maternal care influences hypothalamic-pituitary-adrenal (HPA) function in the rat through epigenetic programming of glucocorticoid receptor expression. In humans, childhood abuse alters HPA stress responses and increases the risk of suicide … These findings translate previous results from rat to human and suggest common effect of parental care on the epigenetic regulation of hippocampal glucocorticoid receptor expression. (p. 342)

Do note that I am not here asserting that Rumbaugh and his colleagues had any inkling of the specificities of the epigenetic mechanisms shared across species that Meaney and collaborators discovered. I refer only to the former's explicit prediction, in the passage quoted earlier in this section, that the influence of environment and early upbringing on primate behavior probably generalizes to other animals. This prediction was neither original nor unique to Rumbaugh and colleagues. But they do tie this familiar point directly to the value of the comparative perspective. And these recent discoveries illustrate that a comparative perspective akin to one Rumbaugh is known for advocating and valuing has been verified by some of the most influential recent results in neurobiology. That field is discovering and in fact extending specifically the effects of rearing and early environment on cognition and behavior in other mammals.

A Strong Commitment to the Comparative Perspective is Necessary for Specific Practices in Laboratory Neurobiology that Use Animal Models to Investigate Human Brain Mechanisms

For my second point, I turn to the work of philosopher of neuroscience Nina Atanasova on the epistemology of animal models in neurobiological research. This is a neglected topic in the philosophy of neuroscience. Most philosophers who have investigated animal models in neurobiology have been interested in ethical concerns. Atanasova's (2015) paper starts with familiar points. Specifically, she agrees that arguments to scientific conclusions based on experiments using animal models are a kind of nondeductive argument, specifically, arguments based on material analogies. **A** (the model) is known to be relevantly materially similar to **B** (the target of research interest) in ways **x**, **y**, **z**,… Possessing features **x**, **y**, **z**,… is relevant to possessing additional feature **f**. Experimentation with **A** reveals that **A** possesses **f**. So probably **B** possesses **f** as well. In the case of standard neurobiology laboratory experiments **B**, the target of ultimate research interest is some human phenomenon, often cognitive or behavioral. **A** is an animal model for human phenomenon **B**. And **x**, **y**, **z**,… and **f** are shared material—biochemical, molecular-genetic, physiological, or

behavioral—features. On some occasions, these shared material properties stand in specific biological relationships (homology, homoplasy). The background of Atanasova's (2015) account is the familiar "scientific textbook" account of animal model usage, particular to neurobiology experiments.

Against this background, Atanasova (2015) offered her important insight. Animal models in neurobiological experiments are often constructed, created, to be relevantly materially similar to the human target phenomena. She wrote:

> In order to be able to extrapolate knowledge from the animal models to [human] conditions, neurobiologists have to first show that what is known about the human conditions, or at least something very similar to them, can be reproduced or simulated in animal organisms. This is the process of model building in which an animal model is designed and developed so that it can simulate the studied condition. (p. 170)

In this context, Atanosova (2015) referred to philosopher Mary Hesse's (1966/1963) well-known work on models and analogies in science. Atanasova pointed out that in this process of designing and developing animal models of human conditions, "the human condition is initially a model for its animal model" (p. 170). Validated use of an animal model to explore a human condition can only occur after this initial design and development of the model: "Only after the human condition has been modeled, or simulated, in the animal model can it be used as an instrument to generate further knowledge that can then be extrapolated back to humans" (pp. 170-171). Philosophical discussions of the epistemology of animal models in neurobiology have not only been rare but have missed this key validation step. Atanasova (2015) wrote, "The philosophical discussion about the validation of extrapolation of knowledge about animal models to human conditions have largely focused on this second stage," namely experiments using the animal models; "however, what makes the extrapolation legitimate happens at the first stage, the stage of model building" (p. 171).

Atanasova's (2015) careful explication of laboratory neurobiology's actual practices of experimentation using animal models is an important contribution to a philosophy of neuroscience that purports to descriptive accuracy. This kind of experimentation is central to neurobiology's current mainstream. But her account is also crucial for my point in this section. Neurobiology purports to discover mechanisms of human cognition and behavior. It routinely uses animal models in its experiments to do this. But as Atanasova (2015) has insightfully shown, its central experimental practices using animal models requires a strong comparative perspective across species. Not only for its extrapolation of experimental results back to human nervous systems, but even more prominently in the design, development, and building of these animal models themselves. Without a strong commitment to a comparative perspective, one akin to Rumbaugh's for psychology, one of neurobiology's most basic experimental tools, the use of animal models in experimental research, could not validly fulfill one of its central explanatory promise: the applicability of experimental results to humans.

If Animal Models Compare Sufficiently to Humans to Justify Generalization of Experimental Results, Then How is it Ethical to do Brain Intervention Experiments on Them? A Strong Comparative Perspective at Work

In the prior section, we saw a strong comparative perspective at work in the use of animal models in contemporary neurobiological experimental practice. This usage and commitment leads immediately to my

third point. Acceptance of a strong comparative perspective and acknowledgment of its value makes one of experimental neurobiology's ethical concerns particularly pressing. Perhaps this ethical concern is neurobiology's most pressing, as it invades the life and work of every lab researcher who does brain intervention experiments on animal models. In a nutshell, if animal models compare sufficiently to target human brain phenomena, especially human cognitive and behavioral brain phenomena, if animal models in many cases are designed, developed, and built to so compare even more closely (see prior section above), and if doing the brain intervention experiments on humans are ethically prohibited, then how is it ethically justifiable to do these invasive experiments using these animals? If animal models resemble and are routinely built to even more closely resemble human cognition in order to justify generalization of results across species, then don't the animals warrant ethical status and consideration about what we can and cannot do to them? After all, for many, it is the marks of human cognition that are among the features that give us ethical standing. And doesn't this concern apply especially to brain intervention experiments in vivo, in which the very mechanisms of cognition and consciousness are manipulated and altered?

Many of the contributors to this volume knew Duane Rumbaugh far better than I did, both professionally and personally. So many had opportunities to know his ethical views and attitudes. Like many practicing scientists, Rumbaugh did not articulate a detailed ethics, at least not in his scientific publications. One exception is a coauthored paper in a volume of proceedings from a conference on great apes and ethics. He and his collaborators stake out a clear Darwinian "continuity" hypothesis for the great apes and humans, and for animals generally, and suggest ethical status for nonhuman animals based on common feelings, intentions, and goals with humans (Rumbaugh, Savage-Rumbaugh, & Beran, 2001). In that chapter, Rumbaugh and collaborators insisted that our unwillingness to attribute the latter commonalities to apes, and animals more generally, leads us to value them only instrumentally. This denies them ethical standing. Ultimately, they insist, this path can lead to a general devaluation even of human life.[2]

Rumbaugh more often expressed his feelings for and deep emotional attachments to nonhuman primates in his more popular writings (see especially Rumbaugh, 2013). These feelings and attachments extended not just to the ones he worked with personally for many years, but also to those living in (threatened) natural environments. He also openly expressed his admiration for these special animals in the media blitzes that surrounded his ape language work.

Of course, these many individual pronouncements do not amount to a detailed ethical framework, from which one can deduce Rumbaugh's assessment of other ethical concerns. But if we couple these expressed affections with his refusal throughout his career to pursue any kind of brain intervention work on any animals and with his predictions expressed in the quotations in the first section above about what he expected to be revealed in future work with non-primates, it certainly seems reasonable to hypothesize that Rumbaugh found much neurobiological experimentation ethically problematic due to the reasoning suggested in the first paragraph of this section.

Admittedly, this hypothesis is speculative. As far as I can gather, Rumbaugh never explicitly ethically rejected brain intervention neurobiology experiments on all animal models, at least not in print. And the kind of research he did involving endangered primates living in enclosed and artificial laboratory environments to study their cognition raises strong ethical hackles for many. Still, there does seem to be one significant

[2] Thanks again to an anonymous reviewer for pointing me to this chapter.

difference. Brain intervention experiments in neurobiology, especially those aimed at discovering the mechanisms of cognition and consciousness, more directly manipulate brain mechanisms than do strictly behavioral studies. Often these brain interventions are intentionally detrimental to the cognition of the experimental animals. Again, I am not here seeking to put words into Rumbaugh's mouth. There is no evidence I can find in print that he reasoned in this fashion. But this is a line that a primate researcher ethically opposed to neurobiological experiments could develop to justify his or her ethical distinction.

I have no novel insights to share about this central ethical dilemma in experimental neurobiology. I only point out that it is one that every neurobiological experimentalist who works with animal models faces, often many times over his or her career. All experimentalists must resolve it to his or her own satisfaction. Many do so only very uneasily. The ubiquity and difficulty of this ethical concern shows how deeply entrenched a comparative perspective is in laboratory neurobiology. Unlike Rumbaugh, many experimental neurobiologists choose to (continue to) pursue invasive brain intervention experiments in mammals, even into the hypothesized mechanisms of cognition and consciousness. Many do so based on general conclusions about science (i.e., that justifying causal-mechanistic explanations of phenomena cannot be done without intervening). I developed this argument with neurobiologist Alcino Silva and neuroinfomaticist Anthony Landreth in Silva, Landreth, and Bickle (2014), although we do not explore any ethical consequences of this feature of experimental science there.[3] These are the ethical considerations to which the value of the comparative perspective in neurobiology leads. Sensitivity to this value and its logical consequences is reflected in this ongoing ethical struggle in the professional life of experimental neurobiologists. There is no escaping this struggle. Every experimentalist must resolve it to his or her own satisfaction. What its centrality to the everyday practices of laboratory neurobiologists shows is that contemporary mainstream neurobiology is as committed to the value of a strong comparative perspective and all that follows from it. Its commitment is to one just as strong and valued as the one to which Duane Rumbaugh and his fellow primatologist revolutionaries were committed.

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[3] I thank a second anonymous reviewer of this manuscript for pushing me on this central ethical concern in laboratory neurobiology. His or her comments improved the final two paragraphs of this section.

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Financial conflict of interest: No stated conflicts.

Conflict of interest: No stated conflicts.

Submitted: *June 15th, 2018*
Resubmitted: *July 8th, 2018*
Accepted: *October 22nd, 2018*