# Extrapolating from Laboratory Behavioral Research on Non-human Primates is Unjustified

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## 1. Introduction

In 2013, the United States' National Institutes of Health (NIH) began phasing out the use of chimpanzees for invasive research. In 2015, the U.S. Fish and Wildlife Service categorized chimpanzees in captivity as endangered, requiring a permit to use them in invasive research.[1]

One reason that the NIH phased out the use of chimpanzees for research was that requests to use the NIH's stable of chimpanzees were rare. Instead, the scientific community was finding other ways to answer the questions that may have also been answered by invasive research on chimpanzees. In other words, they were using other animal models: mice, rats, dogs, pigs, rabbits, and other non-human primates. This phase out was further motivated by the Institute of Medicine's recommendations for the use of chimpanzees in biomedical and behavioral research.[2] They set conditions for acceptable use of chimpanzees in research. For biomedical research, the conditions are that no other suitable model be available, that the research can't be conducted ethically with humans, and that forgoing the use of chimpanzees would significantly inhibit research. For behavioral research the conditions are that the sought insight be otherwise unattainable and that the researchers use acquiescent animals.

Conducting research on animals is supposed to be valuable because it provides information on how human mechanisms work. But for the use of animal models to be ethically justified, it must be epistemically justified. The inference from an observation about an animal model to a conclusion about humans must be warranted for the use of animals to be moral (it's a necessary, but not sufficient, condition of the ethical use of animals for research). In what follows, I am concerned with the epistemology of this inference.

Much has been written on the ethics of research using non-human primates. Most of the debate on the use of animals in research, and especially the use of non-human primates, has been around the ethical appropriateness of such research. Substantially less has been written on the epistemology of using animal models to contribute to knowledge about humans, especially the

epistemic appropriateness of using non-human primates as models. It is often simply assumed that non-human primates are a good research model. Usually when authors object to the use of non-human primates it is on ethical grounds. I object to their use as models on epistemic grounds.

When researchers infer from animals to humans, it's an extrapolation. Animals are obviously similar to humans in some ways and obviously different in others. Extrapolating from animals to humans negotiates these similarities and differences, ideally in a way that warrants a conclusion about humans.[3] For extrapolation to be warranted, research must be thoughtfully designed and analyzed to exploit the similarities and control the differences.

Invasive research on chimpanzees was supposed to provide a good animal model from which researchers could extrapolate information about humans, as the negotiation of the similarities and differences between the model population (chimpanzees) and the target population (humans) was less problematic. But the recent policy changes about the use of chimpanzees for research only impacts their use for invasive research;[4] behavioral research on chimpanzees (and other non-human primates) is still politically unproblematic and widely accepted in the scientific community as a good animal model from which researchers can justifiably extrapolate to target populations. So it's not as though chimpanzees (and other non-human primates) are no longer being used as animal models. It's just that they're no longer being used as animal models in invasive research. They are still widely used as animal models in behavioral research.[5] But, as I argue below, the epistemology of the extrapolation from non-human primates for laboratory behavioral research does not warrant their use as animal models. Laboratory behavioral research on non-human primates is unreliable and so conclusions from it unjustified

In the next section, I identify the goals of conducting laboratory behavioral research on non-human primates and the reasons for selecting non-human primates as models. I then introduce my argument, which is a dilemma, the conclusion of which is that extrapolations from laboratory behavioral research on non-human primates are unjustified. The conclusion is not that extrapolations from non-human primates are unjustified, or even that extrapolations from non-human primates in behavioral research are unjustified. Rather, experimental conditions necessary to conduct the experiment defeat the justification for extrapolated conclusions that result from such experiments.[6]

I do make some uncontroversial epistemological assumptions. One is that there is no *prima*

*facie* justification that animal models are suitable for extrapolation—that they are suitable is a conclusion that needs to be positively supported with evidence. The burden is on the defender of extrapolation from animal models to provide this evidence. This is true not only as a general point about the suitability of animal models but also of every individual study in which animal models are used. I also assume that even if one can provide evidence in support of a claim, this evidence is defeasible, either by further evidence that cuts against the truth of the supporting evidence, or by evidence that the process used to generate the supporting evidence is unreliable (not likely to yield truths).

## 2. Goals of NHP research

There are three goals to conducting laboratory behavioral research on non-human primates. The first is to extrapolate from observations about them to conclusions about human behavior. This is straightforward enough. Researchers induce fear or anxiety into a rhesus monkey and observe its behavior and neural activity. Or researchers play the Ultimatum Game with confined chimpanzees.[7] From these experiments, we are supposed to learn how humans respond to fear or anxiety and how humans respond to perceived unfairness.

A second goal is to use these experiments to extrapolate to a different target population: other non-human primates.[8] Researchers observe an infant rhesus monkey cower in fear and extrapolate that some more general class of non-human primates are likely to exhibit the same behavior.

The third goal builds off both of these extrapolations. Experimental behavioral research on non-human primates generates observations, from which conclusions about all primates can be extrapolated. Such extrapolations are supposed to inform us about how different species evolved. One way this is can occur is by identifying homologous behavior, or similar behaviors in animals that have a common ancestor.[9] Another way this can occur is by identifying convergent behavior, which is when different species exhibit the same behavior as result of environmental factors rather than from having a common ancestor.

So, for example, inducing fear into a variety of non-human primate species and observing the responses may allow one to extrapolate to the claim that all non-human primates of a particular genus exhibit similar behaviors, but that other genii do not. Such a conclusion, if justified, would

be scientifically informative, as it may indicate how fear responses have evolved and, in turn, the evolutionary history of the different species. Similarly, observing a variety of non-human primate species' responses to unfairness may allow one to extrapolate to a conclusion about how our ancestors' and human social psychology has evolved. If justified, these are scientifically informative conclusions.

These are the three targets of extrapolation from laboratory behavioral research on non-human primates: humans, other primates, and general conclusions about primates and how they evolved. As I argue below, the epistemology of laboratory behavioral research on non-human primates fails to support conclusions about any of these targets.

## 3. Why NHP?

There are seven National Primate Research Centers in the United States. At each center behavior and psychology are major areas of research focus.[10] Hundreds of millions of dollars are allocated to them. The implication of this focus at these centers is that the researchers conducting the studies and the administrators funding it believe that laboratory research using non-human primates is valuable. And for it to be valuable, it must be epistemically justified. It may be that not all of this research is extrapolative. Some research may not be intended to generalize to other populations. Instead, some of the research may focus on merely better understanding a specific species under specific conditions. But certainly much of the research is intended to provide a model for extrapolation. Phillips et al. write that "NHPs are used because of their similarity to humans in physiology, neuroanatomy, reproduction, development, cognition, and social complexity."[11] If this is the reason non-human primates are selected, then their use assumes that extrapolative inferences are justified. Further, these similarities are supposed to warrant continued laboratory research on non-human primates, including research on behavior. Laboratory behavioral research in particular is warranted because "Similarities in social and environmental complexity allows for ethologically relevant input to behavioral paradigms for social cognition."

Whether one animal is similar to another depends on what properties of the animals one is interested in, or which properties are relevant. [12,13] For the present purposes, it is enough to note that a variable can be causally relevant by inhibiting a certain effect, whether it causes it or not.

Non-human primates are supposed to be similar to humans in many relevant ways but not different in relevant ways, and are far more accessible than humans to subject to research. The science would be best if humans could be used. But for various reasons, humans are not accessible, usually because it would be unethical to use them. But other animals such as rats, pigs, dogs, mice, rabbits, and non-human primates can be bred, sold, confined, manipulated, and euthanized, all relatively cheaply. And they'll never miss a follow-up visit. They are logistically, ethically, and fiscally more accessible than human subjects.

Indeed, many non-human primates are small enough to keep and breed in normal-sized buildings; and their disposal does not typically raise alarm. Even the great apes can spend their lives under confinement and control much more cheaply than humans can be. Yet they are supposed to be similar enough to humans that extrapolation from observations regarding them are supposed to provide strong evidential support for conclusions regarding humans.

## 4. The dilemma

Laboratory behavioral research on non-human primates cannot provide a suitable model about which observations can be extrapolated to a target population, whether that target population is humans, other non-human primates, or to draw general conclusions about the history and evolution of species. The argument can be stated in the form of a dilemma. The dilemma is: (a) either non-human primates exhibit a relevant dissimilarity or they don't; (b) if they don't exhibit a relevant dissimilarity, then experimental conditions introduce a causally relevant variable, which confounds the results; (c) if they do exhibit a relevant dissimilarity, then the results cannot be generalized; thus, (d) either the results are confounded or they are not generalizable, which is to say that extrapolation is not justified.

Here is another way to put the point. Hoff and Stiglitz argue that there are two strands of behavioral economics.[14] The first strand conceives of agents as quasi-rational actors whose behaviors are driven not only by incentives, but also by the context in the moment of the decision. Such contexts may be able to drive a wedge between the decisions that result from "slow" and "fast" thinking. The second strand conceives of agents as enculturated actors, actors whose preferences, cognition, and perception are not only shaped by "fast" and "slow" thinking, but by cultural mental models. According to this strand, what drives behavior is not limited to

incentives and context, but also includes the actor's experience and exposure.[15] These in turn create cultural mental models, which partly determine what aspects of a particular context will influence behavior. Hoff and Stiglitz offer compelling empirical evidence supporting this second strand of behavioral economics.

This distinction between strands is an instance of the dilemma above. If agents are enculturated and behavior is driven by experience and exposure, then unless the model and targets share the same experience and exposure, extrapolation from model to target will be confounded by the different social constructs influencing each population's behavior. I'm claiming that the conditions of laboratory behavioral research guarantee that the experience and exposure differ between any model population and the target for extrapolation. The laboratory conditions change the experience and exposure of the non-human primate.

One might argue that while non-human primates and humans are relevantly similar in that they are enculturated, laboratory settings don't introduce causally relevant variables. The thought is that premise (b) above is false. However, this is tantamount to the claim that if humans were subjected to conditions similar to those found in the laboratory, being so subjected would not be causally relevant to human behavior. That is, being confined, coerced, separated socially, etc. would not alter behavior. If laboratory conditions are not causally relevant for non-human primate behavior, and non-human primates and humans are not relevantly different, then laboratory conditions are not causally relevant for human behavior. But we know that conditions resembling those of the laboratory (e.g., prison) are causally relevant to human behavior. Thus, it can't be true that non-human primates are relevantly similar, that laboratory conditions are not causally relevant, and that conditions similar to those of the laboratory are causally relevant to human behavior. One of these propositions must be false. By stipulation the first proposition is true. The third proposition is empirically supported (see below). That only leaves the second proposition—that laboratory conditions are not causally relevant.

The alternative is the other horn—that non-human primates are not enculturated agents. But then non-human primates would be a poor model for extrapolation. They'd be a poor model to extrapolate to humans, because humans *are* enculturated. And they'd be a poor model to extrapolate to other non-human primates for the purposes of identifying convergent or homologous behavior because we would know that behaviors in non-human primates have different drivers than behaviors in human primates—there would be at least two different

mechanisms at work—which defeats the pursuit of convergent or homologous behavior. Either way, the conclusions that result from extrapolations of observations of non-human primate behaviors in laboratory research are unjustified.

### 4.1 The dilemma and chimpanzees

Researchers have recently been experimenting on the behavior of chimpanzees using methods from behavioral economics. The experiments are supposed to measure moral psychological states and how choices are ordered. For example, researchers have played the Ultimatum Game with chimpanzees (among other species).[16] The Ultimatum Game is played between two agents, a proposer and a responder. The proposer is endowed with some valuable fund. The proposer's role is to offer a split of this fund with the responder. If the responder accepts, each agent receives their share of the proposed split. If the responder rejects the proposal, neither agent gets anything. The game is supposed to measure sensitivity to social goods such as fairness and cooperation.

When the game is played with humans, the players must consent to participation. Setting aside the fact that the research would not get past an institutional review board without requiring participant consent, even if it could the observations would be of little value. Games such as the Ultimatum Game yield valuable results because participants' behavior in them is not coerced. The absence of coercion is guaranteed only by an appropriate informed consent process. Without such a process, the participant's behavior (his or her choices) cannot be interpreted as representative of his or her sensitivity to social or moral norms[17], as it is plausible that their choices are influenced by their forced participation. Forced participation is a causally relevant variable in experimental economics.

When chimpanzees (or any other non-human primate) play the Ultimatum Game (or any other similar game), can they consent to participation in the research? In other words, are they relevantly similar to humans in that they can consent? Or do they lack such a capacity and exhibit a relevant dissimilarity? Either way, extrapolation from observations from this research is not justifiable.

In laboratory settings, chimpanzees do not provide consent to participate in research. If they are relevantly similar to humans and have the capacity to consent, then the experimental

conditions introduce a causally relevant variable that confounds the results. Whatever the observations are, if chimpanzees have the ability to consent, then there is no way to determine whether the observations are due to social behavior of chimpanzees or due to social behavior of chimpanzees *and* their forced participation. It would therefore not be possible to extrapolate to a target population that has the capacity to consent and whose participation is voluntary and informed.

However, if chimpanzees lack the ability to consent, then the experimental conditions don't introduce a causally relevant variable. Instead, the chimpanzees exhibit a causally relevant dissimilarity. Having the ability to consent is necessary for having autonomy. If chimpanzees lack the ability to consent, then they don't have autonomy[18]. But in humans, autonomy also grounds our choices. For example, when humans play the Ultimatum Game, our behavior is a result of our making choices compatible with our freedom and power to do so and the preferences that emerge from our will—they result from our autonomy. When a person rejects an offer of 20% of the endowment, that's an autonomous choice. If chimpanzees lack the ability to consent and so autonomy, then the source of their choices is a different mechanism than it is in humans. And if their behavior results from a different mechanism, then there is a causally relevant dissimilarity between chimpanzees and the population that is the target of the extrapolation. This causally relevant dissimilarity defeats the extrapolation from model to target. Thus, the extrapolation from chimpanzees to humans is either confounded or defeated. Either way, the inference is not justified. The only way an extrapolation from these observations can be justified is if the conclusion reached is about a population not relevantly dissimilar, such as imprisoned humans or other confined non-human primates. The alternative is to assert that the fact of confinement does not modulate observed behavior. This assertion, however, implies that such animals are poor models for extrapolation, since we know imprisonment can change cognition and behavior.[19]

One might object that whether autonomy or freedom grounds human behavior is precisely what is under investigation when researchers play social preference games with chimpanzees, which means I can't simply assume that human behavior is so grounded. This objection provides a useful foil for my argument. So long as human behavior is enculturated—so long as it is influenced by experience and exposure—the extrapolation is unjustified. If human behavior is enculturated, and chimpanzee behavior is not, then model and target are relevantly dissimilar,

which defeats the extrapolation. But if, like it is in humans, chimpanzee behavior is enculturated, then laboratory conditions introduce a confounding variable, which defeats the extrapolation from model to target. Thus, denying that human behavior is grounded by autonomous or free choice doesn't free one from the dilemma.

Even if human behavior is driven not by autonomous or free choice but merely by neurochemistry (presuming, maybe falsely, that freedom and neurochemical explanations of behavior are incompatible), so long as in humans experience and exposure act upon that neurochemistry, the problem remains. [20] The only way to avoid the dilemma entirely is to claim that laboratory conditions don't introduce a confounding variable, because neither chimpanzee nor human behavior is influenced by experience and exposure. If that were true, one may justifiably extrapolate from chimpanzees in the lab to humans outside of it. But the defender of the claim that human behavior is not influenced by experience and exposure bears the significant burden of establishing it.

Consider the Institute of Medicine's recommendations for conditions under which using chimpanzees as subjects is acceptable. The first condition is that the knowledge be unattainable by other means. The second, however, is that the animal be acquiescent. Animals are acquiescent when they don't "refuse or resist research-related interventions and that do not require physical or psychological threats for participation."[21] Of course, failing to refuse is not the same as consenting, particularly when the animal is confined and has been previously compelled. It's fantasy to think that because a chimpanzee acquiesces to participation they are therefore "consenting" to participation, that distress is minimized, and that any confounders are controlled. It's not difficult to imagine that a chimpanzee who has been "retired" to a particular facility but has been a subject in many other studies acquiescing to research because of their previous experience and exposure. My point is that whatever experience and exposure they have been subjected to previously affects not only whether the animal acquiesces, but also the behavioral outcome of interest, and this influence confounds extrapolation. The alternative is to hold that the chimpanzees' experience and exposure do not so influence. But in that case the extrapolation is undermined by a relevant dissimilarity between the chimpanzee and the target, because in humans such behavior is influenced by experience and exposure.

For example, Proctor et al. played the Ultimatum Game and the Dictator Game.[22] The Dictator Game is similar to the Ultimatum Game, except that the recipient of the offer does not

have the opportunity to reject the proposal. They hypothesized that chimpanzees would propose more equal splits of tokens in the Ultimatum Game than in the Dictator Game, as there is a cost of having a proposal rejected in the Ultimatum Game, but no such cost in the Dictator Game. They found that chimpanzees proposed more equal splits in the Ultimatum Game. They validated this finding by conducting a similar experiment with children, concluding that the behavior is in common between chimpanzees and humans.

However, no such extrapolation is epistemically justified. In addition to the fact that chimpanzees and humans exhibit a relevant dissimilarity in their ability to consent,[23] it is possible that the children, as they often are in research, were sensitive not to the allocation of goods but to cues from authority figures. Similarly, the chimpanzees may have been also sensitive not to the allocation of goods, but to cues from authority figures. This needs to be controlled for any extrapolation to be justified. Second, the Ultimatum Game incorporates potential punishment for offering an unacceptable split. Both chimpanzees' and the children's past experience and exposure to punishment plausibly influenced their risk aversion. This needs to be controlled for any extrapolation to be justified. Third, the Ultimatum Game, but not the Dictator Game, is subject to framing effects—the words used to describe the behaviors to the players impact their behavior.[24] If the children's behavior was framed by the words used to describe the game, then there is clearly a relevant dissimilarity between chimpanzee and human, as the game is not communicated to chimpanzees in the same way as it is to humans (this is not to say that chimpanzees' behavior is not framed by how it's communicated). More generally, because experience and exposure *do* influence a child's social behavior, experience and exposure need to be controlled across species. The alternative is to hold that they are relevantly different populations, which also undermines the extrapolation. In light of these considerations, any similarity in behavior looks accidental.

The dilemma also defeats laboratory research in behavioral genetics and behavioral neuroscience using chimpanzees as models. Researchers have identified the gene AVPR1A as being associated with various behaviors. AVPR1A codes for a receptor of neuropeptide hormone arginine vasopressin (AVP). Researchers look for variations of this gene and associations this variation may have with behavioral observations. For example, some researchers observe chimpanzees' "joint attention," or their ability to communicate in a way that brings another agent's attention to a stimulus of common interest.[25] Others observe aggression and dominance,[26]

sociability,[27] or personality.[28] They find that variation in AVPR1A can account for some of the variation in behavior. The goal is to identify the genetic basis of primate social behavior.

The problem is not that the results form a particular study are questionable. Whether variations in AVPR1A can explain some percentage of the variation in behavior among the chimpanzees is beside the present point. The problem is in extrapolating from those results. It's impossible to extrapolate from the observation that some percentage of the variation in behavior is due to variation in AVPR1A to the conclusion that AVPR1A grounds variation in behavior in other primate species, because for extrapolation the relevant observation isn't merely the percentage of variation accounted for. The relevant observation is that *variation in AVPR1A accounts for some of the behavioral variation under that cultural mental model*. Unless experience and exposure is held fixed from model to target, any extrapolation from model to target will be confounded.

Further, laboratory conditions require that the subjects have experienced significant stress, perhaps from confinement and compulsion, or from past trauma. And stress interacts with the release of AVP.[29] Thus, the conditions required to conduct the experiment introduce the confounding variables. In the absence of controlling for experience and exposure, it's impossible to conclude that another primate species' behavior would be accounted for by genetic variation at all. It's conceivable that some experiences or exposures would overwhelm entirely any genetic driver of behavior. Or suppose that a given cultural mental model results in little variation of behavior. In that case, with little behavioral variation to account for, it would be impossible to say that variations in AVPR1A account for any variation in behavior. It's also possible that in different cultural mental models the percentage of variation in behavior accounted for would be greater. Similarly, it's possible that chimpanzees' cultural mental model (for example, the model that results from the stress from confinement or trauma from past research compulsion) interacts epigenetically with AVPR1A.[30]

That's the first horn. But one might think that the extrapolation from chimpanzee to human isn't confounded, because chimpanzees' behavior isn't influenced by cultural mental models in the way that other primates' behavior is so influenced. The second premise (second horn) is that if the chimpanzees in the research are relevantly dissimilar, then the extrapolation is not generalizable. There would be a relevant dissimilarity, because for humans not only do experience and exposure influence behavior like sociability, but also high levels of stress and

chaos influence social behaviors epigenetically.[31] If chimpanzees aren't like this, then their behavior and humans' behavior have different drivers, which is a relevant dissimilarity. If chimpanzee behaviors and human behaviors have different drivers, then there is good reason to believe that what is true of chimpanzee behavior is a poor indicator of what is true of human behavior, which defeats the extrapolation.

This is true even if their observed behaviors are similar. Suppose that two people arrive at King's Cross station, one by rail and one by tube. They're both in the same place, but by way of different mechanisms. Studying how one of them arrived at King's Cross to discover that she arrived by rail does nothing to tell us how the other (or anyone else also at the station) arrived. Similarly, if to avoid the first horn one holds instead that chimpanzee (or any other non-human primate) behavior and human behavior have different drivers (one for which experience and exposure are important), then studying one to learn about the other—even if their observed behaviors are the same—is like studying how one traveler arrived at King's Cross to learn how the other arrived.[32]

It's not merely social behavior that genetics are supposed to account for. Other research indicates that variation in non-human primates' fine motor skills and tool use can be explained genetically.[33] This research faces the same dilemma, however. There's strong evidence that the experience and exposure of human children affects various aspects of development. For example, chaos and trauma influence not only cognitive development, but also fine and gross motor skills.[34] Further, strong parental nurturing doesn't mitigate this influence. If chimpanzees are similar to humans in this regard, one would expect that the past trauma to social location and bodily integrity or the confinement and compulsion influence the development of fine and gross motor skills, as it would in human children.[35] If so, then when one observes chimpanzees manipulate a tool in the laboratory, there's no way to know whether the behavior is due to genes or due to genes and the cultural mental model that has developed from their experience and exposure. If cultural mental models so confound, then it's impossible to extrapolate any association to other species that behave within a different model. The laboratory conditions (e.g., trauma, confinement, compulsion, social disruption) introduce causally relevant dissimilarities, which confound any extrapolation.

The alternative is to hold that these laboratory conditions don't confound. In that case, chimpanzee behavior has a relevantly different driver than human behavior, which undermines

the extrapolation. Either way, the extrapolation is not epistemically justified.

In the case of behavioral economics and behavioral genetics, laboratory conditions introduce variables (social disruption, trauma, confinement, compulsion, stress, and the resulting cultural mental models) that confound the inferences one could make from the observations of behavior, defeating the extrapolation. The only way to avoid this confounding is to assert that experience and exposure don't influence chimpanzees' behaviors in the way that they do humans. But in that case there is a relevant difference between chimpanzees and humans, which defeats the extrapolation from the model to the target. Behavioral neuroscience faces the same dilemma.

In their report on using chimpanzees in biomedical research, the Institute of Medicine uses as an example of licit research a study looking at the neurological homology of joint attention in humans and chimpanzees. In humans the area of interest is Broca's area, which is asymmetrical and enlarged on the left side of the brain and activated by vocalization and gestures, the behaviors common to initiating joint attention. The study imaged the brains of chimpanzees while being presented with a stimulus know to provoke attempts at initiating joint attention.[36] They found similar patterns of activation as those found in humans.

This study was an example of laboratory behavioral research on chimpanzees, but it wasn't extrapolative. That is, the chimpanzees in this study were not being studied as a model for a target population. So the present dilemma doesn't undermine the epistemology of this research, though there still might be reasons to think that the study introduced confounding variables, such as those that result from the manipulation of their experience and exposure. However, the Institute of Medicine concludes that "The presence of similarly activated underlying brain structures would suggest that chimpanzees could be used to model human communication development."[37] While this study may not itself be extrapolative, the IOM is explicit that others can use chimpanzees as a model for human communication. These further studies would be undermined by the present dilemma. Indeed, making explicit the chain of inferences clarifies the effect of the dilemma.

The first inference is that since one type of communication is associated with activation of the same region of the brain in both humans and chimpanzees, chimpanzees and humans are similar in one relevant way. Using the chimpanzee as a model for the neurobiology of human communication, researchers then observe associations between images of the brain, for example, and communication behavior in chimpanzees. The next inference is that since chimpanzees are a

good model and some association (whatever it happens to be in a particular study) obtains between neurobiology and behavior in them, a similar association obtains in human. But it's this second inference that the dilemma undermines. It's undermined because if chimpanzees are relevantly similar to humans as the IOM asserts, then it's plausible that their experience and exposure influence their communication behavior. It doesn't take a well controlled experiment to know that a human being's experience and exposure—and even their local environment—influence their communication behaviors. If chimpanzees are relevantly similar, then it's plausible that their experience and exposure influence their communication behaviors and thus any observed association those behaviors may have with imaged brain states.

In some research the chimpanzees being researched are in sanctuaries or facilities that attempt to mimic heir natural environment. However, thinking that because a subject is at the time living in a facility that resembles their natural environment we don't need to worry about confounding ignores the influence that past experience and exposure can have on behavior. Chimpanzees who are in sanctuaries are usually chimpanzees who have been retired from research or who have otherwise experienced trauma. There is perhaps no better guarantee that experience and exposure will confound extrapolation than to use chimpanzees who have lived chaotic, traumatic, and injured lives, unless the extrapolation is to a target that has had similar experience and exposure.

I have only provided a few examples of laboratory behavioral research using chimpanzees extrapolation from which the dilemma undermines. But the problem generalizes:
Any laboratory research that has an observation of chimpanzee behavior as the dependent variable will either be confounded by the subjects' experience and exposure or be defeated by a causally relevant dissimilarity. This makes extrapolation impossible. And since extrapolation is impossible, there is very little knowledge to be gained.

Using chimpanzees in behavioral research as models from which to extrapolate is not epistemically justified. The *ethical* justification for their use requires balancing the epistemology of their use with the animals' welfare. I am only arguing that the epistemology of using them as animal models from which to extrapolate suggests there is nothing to be learned. If there is nothing to be learned, then any net harm to the animal will outweigh the benefits of their use, which implies that it is unethical to use them as animal models. Furthermore, some of the factors that harm the animals (e.g., confinement and coercion) may also undermine the epistemology.

But I am only concerned with these factors to the extent that they undermine the epistemology. Beyond the fact that the things that harm the animals may be the things that also undermine the epistemology of extrapolation, the welfare of the animals is irrelevant to the present purpose.

### 4.2 Other non-human primates

That the dilemma undermines extrapolations from well designed research using the animal thought to be most similar to humans suggests that it will also undermine extrapolations from more poorly designed research using less similar animals. Rhesus monkeys are commonly used as models, and a common type of experiment is the human intruder test. In the human intruder test, the animal is caged, then a human approaches the cage. Variations on the disposition of the human allow for manipulation of the experimental conditions. Responses, as measured by behavior or biometrics, are observed.

Rhesus monkeys are presumably selected because they bear relevant similarities to target populations, such as other non-human primates or humans. These similarities presumably include similar psychologies. That is, the reason rhesus monkeys are chosen for experimentation using the human intruder test is that they are psychologically similar to the target population. The human intruder test requires that the animals be confined. We know that confinement affects the psychology of members of the target populations.[38] If the rhesus monkey doesn't exhibit any relevant dissimilarities, then their confinement can be expected to affect their psychology, though maybe not in exactly the same way as it does in the target population. If the observation of interest is causally relevant to confinement, then the experimental conditions introduce a variable that is causally relevant. And doing this confounds the results.

Suppose that the experiment calls for a stranger to approach the cage, and the observation is whether the animal retreats, maintains its position, or moves to the front of the cage. When the stranger approaches the cage and the animal is observed retreating, there is no way to distinguish whether this is due to anxiety about strangers or anxiety about strangers *and* being confined. In other relevantly similar animals, being confined interacts with anxiety just as other experience and exposure interact with the communication behaviors or sociability. If rhesus monkeys are relevantly similar, there is no way to eliminate this possibility. That is, whatever the observation is, there is no way to determine whether the observation is due to the independent variable or to

the conjunction of the fact that the animal is confined *and* the independent variable. If the observation is so confounded, then there is no justification to extrapolate from these observations to a target population that isn't confined.[39]

However, if the rhesus monkey is unlike other species, such as humans, and being confined has no effect on its behavior, then they exhibit a causally relevant dissimilarity (in humans, confinement has certain downstream effects on behavior). If they exhibit causally relevant dissimilarities, then one cannot justifiably extrapolate from those observations to target populations that are so relevantly dissimilar, such as humans, chimpanzees, or any other animal for whom confinement affects behavior. Either way, then, one cannot extrapolate from observations of the rhesus monkey in the human intruder test to humans (even if the observation is something as simple as cortisol level).

Another example of rhesus monkeys being used in laboratory behavioral research is a recent study investigating the effect of oxytocin on their ability to recognize faces. Oxytocin is a neuropeptide implicated in a wide range of social behaviors. Researchers found that in rhesus monkeys oxytocin did affect their facial recognition.[40] But the laboratory conditions confound any useful inference. In humans, oxytocin makes social cues more salient.[41] But being separated and confined plausibly also affects which social cues are salient. Indeed, it takes mental gymnastics to think that oxytocin might change social behavior but also think that confinement and coercion don't. The study assumes that rhesus monkeys, like humans, are affected by administration of an intranasal neuropeptide but that they aren't affected by their experience and exposure. If both of these assumptions are true, then the rhesus monkey's social behavior operates differently than a human's, because human behavior *is* affected by experience and exposure.

Confinement to a cage introduces a confounding variable in animals that are potential target populations for extrapolation from non-human primate research. One could ease this confounding by not confining the animal. Some researchers do this, producing results from which one can extrapolate but that are logistically and experimentally difficult to acquire. Thus, some animals that are supposed to be relevantly similar to humans, such as chimpanzees, bonobos, and orangutans, are confined not to cages but larger research centers that more closely resemble their natural environments.

For example, Parker et al. conducted a study on AVP concentration and sociability of rhesus

monkeys, but the monkeys were all born and bred in large outdoor facilities within complex social groups.[42] Their hypothesis was that there would be a difference in AVP concentration in cerebrospinal fluid between low-social monkeys and high-social monkeys. The behavioral outcomes in this study were ethological observations of sociability (e.g., grooming, play). They found that AVP concentration could discriminate between low- and high-social monkeys. However, even in such well designed studies (this is likely as good as a controlled environment can get), the dilemma undermines the extrapolation. While the physical environment may have been very similar to the monkeys' natural environment, and the monkeys were born and bred in it, the social environment was artificial, and this may influence the sociability of individual monkeys. Also, while the study made the behavioral observations prior to collecting the sample, collecting the sample plausibly influenced the monkey's subsequent sociability—it's plausible that being caught in their home, drugged, and tapped in a lab for cerebrospinal fluid influences subsequent behavior so that future behavioral observations are potentially confounded by earlier research participation. It's not clear whether the monkeys in this study had participated in previous research and if so, what those conditions were.

The reasons that we use non-human primates are at odds with what we hope to learn by studying their behavior under experimental conditions. There is tension between the reasons for their accessibility (e.g., they're easy to confine, compel, injure, breed, euthanize) and the conclusions we intend to draw about the behavior of other primates outside of experimental conditions. Anytime an animal model is chosen because of some relevant similarities it bears to a target population, and the experimental conditions manipulate those similarities in the model but not the target, researchers will face the above dilemma. This true of all animal models, not just non-human primates. For example, if a Fischer rat is chosen because it metabolizes a certain drug like humans do, then if the experimental conditions manipulate that metabolism in the rat, then either the subsequent extrapolation would be confounded or the rat would actually bear a relevant dissimilarity to humans.

## 5. Potential Targets

If non-human primates are being used as animal models, what, then are suitable target populations to which one can extrapolate? The answer will of course depend on the relevant

similarities and differences between model and target. To control for experience and exposure, the target population would have to have had similar experience and exposure. Humans who may exhibit few relevant dissimilarities are those who have spent significant time confined, such as prisoners. However, prisoners are a highly protected group of people, and it's unlikely they will have been exposed to participation in so much research. Another population that might exhibit fewer relevant dissimilarities in experience and exposure are children who have been removed by various states from their families and placed in artificial social environments, such as children of Indigenous Peoples, Aborigines, or Latin American immigrants attempting to cross the United States' southern border. However, such populations' confinement is typically temporary, which is likely to produce relevant dissimilarities in cultural mental models. Notwithstanding the significant ethical standards research on these populations would violate, it's unlikely that any such extrapolation from non-human primates in the laboratory to humans will be epistemically justified.

Above I mentioned that one of the purposes of laboratory behavioral research on non-human primates is to establish the evolutionary history of primate behavior. The above argument has implications for this pursuit. Indeed, it seems to entail that it is impossible to ever discover that behavior is homologous or conserved through evolution from species' common ancestor. How would researchers make such a discovery in the laboratory? It would require that the species that are supposed to exhibit the homologous behavior all respond to the laboratory conditions in a similar way. Since we know that these conditions can influence human behavior, for this behavior to be homologous other species' behavior would also need to be similarly influenced. But, as above, this confounds the observations and undermines the inference that the observed behavior is homologous.

The alternative is that some species' (i.e., humans) behavior is influenced by the laboratory conditions, and other species' is not. If this is true, then this dissimilarity would fail to support an inference that the observed behavior is homologous and may instead support convergence, if anything.

## 6. Conclusion

I do not argue that all extrapolation from non-human primates is epistemically unjustified.

The above argument only threatens the epistemology of laboratory behavioral research on non-human primates that uses non-human primates as animal models. It undermines the extrapolation, so if some laboratory behavioral research on non-human primates infers its conclusions some other way, then this research is unaffected by the above argument. For example, some research may use non-human primates to generate hypotheses rather than provide a model from which to extrapolate to a target population. The above argument would not undermine such research. However, if testing these hypotheses inevitably requires testing them on non-human primates who are then used as models from which to extrapolate, then it's not clear that even this exploratory research is epistemically justified.

Extrapolating from observations of non-human primates acquired by way of field experiments or ethological observation is also not threatened, so long as the conditions of research don't introduce other confounding variables. Field or ethological research may even provide the best models for extrapolation, given that the observed behaviors occur in the species' natural environment.[43] There may be other epistemological reasons to be dubious of research outside of the lab. And there may be ethical and logistical reasons why such research either shouldn't or can't be conducted. But I have not identified any of these. The above argument is merely an epistemological argument that extrapolation from non-human primates in laboratory behavioral research is not justified.

The above argument also doesn't address the epistemology of invasive biomedical research on non-human primates. Such research is not likely to continue to occur using chimpanzees, but it is still commonplace for other species to be used as animal models. I discussed briefly above some of the epistemological problems with using animal models that others have identified, but I don't add anything. However, if ever animal models are used based on a similarity to the target, and the experimental conditions of the research manipulate that similarity in the model, the research will face the dilemma identified above. For example, Garner provides an impressive list of all of the ways in which caged environments of mice and rats influence the values of dependent variables in biomedical research. He writes further that "animals in barren, uncontrollable environments are models of chronically stressed, socially isolated, and immune-suppressed humans; but, if we want good models of most human cancer patients receiving physical and social supportive care, then we need to think carefully about the social and physical enrichment of these animals."[44] I am arguing that the same is true of behavioral research using

non-human primates.

Garner also argues that the development of animal models in behavioral neuroscience, presumably including those using non-human primates, ought to adopt methods of human clinical trials so that the failure rate of translational research is not so high. However, if animal models are adapted so that they more closely resemble human clinical trials, it is difficult to see how these can be carried out in the laboratory. Human clinical trials do not typically confine and compel their subjects or significantly disrupt their social lives; they don't trap and drug or otherwise impose significant interventions on subjects' experience and exposure. Behavioral research that more closely resembles human clinical trials would look very much like field research—observing non-human primates in their natural environments and social locations.[45]

The epistemology of using non-human primates as animal models in laboratory behavioral research informs the ethics of using them. The ethical justification for any research that requires subjects to bear a burden is that the research provide a benefit. The burden must be proportional to the expected benefit. The epistemology of extrapolation from laboratory research using non-human primates says there's nothing to be gained. If there's nothing to be gained, then there is little ethical justification for using them as research subjects.

[1] Kaiser J (2015) NIH to end all support for chimpanzee research. *Science*. DOI: 10.1126/science.aad7458.

[2] Shelton-davenport MK, Kahn JP. (2011) Chimpanzees in Biomedical and Behavioral Research. *National Academies Press.* Available from: http://www.nap.edu/catalog/13257

[3] Extrapolation is not necessarily from animal models to humans. It's any instance of inferring from a population that bears similarities and differences to the target population.

[4] The recent policy changes do not affect the use of other non-human primates for invasive research.

[5] National Primate Research Centers' Areas of Research Using Nonhuman Primates. https://nprcresearch.org/primate/research.php. Accessed August 24, 2018.

[6] There are few detailed accounts of extrapolation. See for examples LaFollette H and Shanks N (LaFollette H and Shanks N (1993) Animal Models in Biomedical Research: Some Epistemological Worries. *Public Affairs Quarterly* 7(2): 113–130.; LaFollette H and Shanks N (1995) Two Models of Models in Biomedical Research. *The Philosophical Quarterly (1950-)* 45(179): 141–160. DOI: 10.2307/2220412.; LaFollette H and Shanks N (1996) *Brute Science: Dilemmas of Animal Experimentation*. Brute Science: Dilemmas of Animal Experimentation.

Routledge.; Steel D (2007) *Across the Boundaries: Extrapolation in Biology and Social Science*. Environmental Ethics and Science Policy Series. Oxford University Press.; Cartwright N (1989) *Nature's Capacities and Their Measurement*. Oxford University Press.; Degeling C and Johnson J (2013) Evaluating animal models: Some taxonomic worries. *Journal of Medicine and Philosophy (United Kingdom)* 38(2): 91–106. DOI: 10.1093/jmp/jht004.

[7] Proctor, D., Williamson, R. A., de Waal, F. B. M., & Brosnan, S. F. (2013). Chimpanzees play the ultimatum game. *Proceedings of the National Academy of Sciences*, *110*(6), 2070–2075. https://doi.org/10.1073/pnas.1220806110

[8] Rajala, A. Z., Reininger, K. R., Lancaster, K. M., & Populin, L. C. (2010). Rhesus Monkeys (Macaca mulatta) Do Recognize Themselves in the Mirror: Implications for the Evolution of Self-Recognition. *PLoS ONE*, *5*(9), e12865. https://doi.org/10.1371/journal.pone.0012865

[9] Brosnan SF (2013) Justice- and fairness-related behaviors in nonhuman primates. *Proceedings of the National Academy of Sciences* 110(Supplement_2): 10416–10423. DOI: 10.1073/pnas.1301194110.; Brosnan SF, Talbot C, Ahlgren M, et al. (2010) Mechanisms underlying responses to inequitable outcomes in chimpanzees, Pan troglodytes. *Animal Behaviour* 79(6): 1229–1237. DOI: 10.1016/j.anbehav.2010.02.019.; Brosnan SF, Beran MJ, Parrish AE, et al. (2013) Comparative approaches to studying strategy: Towards an evolutionary account of primate decision making. *Evolutionary Psychology* 11(3): 606–627. DOI: http://dx.doi.org/10.1177/147470491301100309.

[10] Op cit note 5

[11] Phillips KA, Bales KL, Capitanio JP, et al. (2014) Why primate models matter. *American journal of primatology* 76(9). NIH Public Access: 801–27. DOI: 10.1002/ajp.22281.

[12] Op cit note 11

[13] More specifically, it depends on which properties are causally relevant. Criteria for causal relevance are difficult to identify. What is clear is that *A* can be causally relevant to *B* by not only causing, or promoting, *B* but also by preventing, or inhibiting, *B*. It's possible for *A* to not cause *B*, but still be causally relevant to it in virtue of its preventing it. Further, *A* can be causally relevant to *B* if it merely inhibits it, and doesn't prevent entirely, such as when an inhibition of *B* varies according to dosage of *A*. If in the animal model *A* promotes *B* but in the target animal *A* doesn't promote *B*, and *B* is causally relevant to the outcome of interest, then the animal model and target animal are relevantly different, weakening any extrapolation from model to target. Likewise, if in the animal model *A*'s promotion or inhibition of *B* is dose-dependent, and *B*'s promotion or inhibition in the target animal exhibits a different dose-dependency, then the model and target are again relevantly different, weakening any potential extrapolation. Op cit note 6 Steel D (2007) for a detailed account of causal relevance.

[14] Hoff K and Stiglitz JE (2016) Striving for balance in economics: Towards a theory of the social determination of behavior. *Journal of Economic Behavior & Organization* 126: 25–57. DOI: 10.1016/j.jebo.2016.01.005.

[15] One might wonder what work "exposure" is doing. An animal may be exposed to features of an environment without experiencing them, and it's possible that being so exposed influences that animal's behavior. An obvious example of this is when a person's local environment is polluted with industrial emissions that are perceptually undetectable. These are exposures that may influence a person's behavior, but they aren't experienced.

[16] Op cit note 9 (Bronson 2013); Smith P and Silberberg A (2010) Rational maximizing by humans (Homo sapiens) in an ultimatum game. *Animal Cognition* 13(4). Springer-Verlag: 671–677. DOI: 10.1007/s10071-010-0310-4.

[17] There is one way: conduct the research without the participants knowing they are participating in an experiment.
[18] For example, when someone is medically compromised and lacks the ability to consent to treatment, the person also at that same time lacks autonomy. It is in respect of their past and future autonomy that medical decisions are made based on what the person would want, if he or she had autonomy and could make a decision.
[19] Adams K (1992) Adjusting to Prison Life. *Crime and Justice* 16. The University of Chicago Press: 275–359. DOI: 10.1086/449208.; Bukstel LH and Kilmann PR (1980) Psychological effects of imprisonment on confined individuals. *Psychological Bulletin* 88(2): 469–493. DOI: 10.1037/0033-2909.88.2.469
[20] Thanks to an anonymous referee for this raising this objection and the offered response.
[21] Op cit note 2 p. 62
[22] Op cit note 7
[23] Children can't consent, but they can assent. Chimpanzees may be able to assent, but laboratory conditions undermine the idea that chimpanzees are assenting, because they are coerced. Rather, they are are acquiescing.
[24] Dreber, A., Ellingsen, T., Johannesson, M., & Rand, D. G. (2013). Do people care about social context? Framing effects in dictator games. *Experimental Economics*, *16*(3), 349–371. https://doi.org/10.1007/s10683-012-9341-9
[25] Hopkins, W. D., Keebaugh, A. C., Reamer, L. A., Schaeffer, J., Schapiro, S. J., & Young, L. J. (2014). Genetic Influences on Receptive Joint Attention in Chimpanzees (Pan troglodytes). *Scientific Reports*, *4*, 1–7. https://doi.org/10.1038/srep03774
[26] Wilson, V. A. D., Weiss, A., Humle, T., Morimura, N., Udono, T., Idani, G., … Inoue-Murayama, M. (2017). Chimpanzee Personality and the Arginine Vasopressin Receptor 1A Genotype. *Behavior Genetics*, *47*(2), 215–226. https://doi.org/10.1007/s10519-016-9822-2
[27] Staes, N., Koski, S. E., Helsen, P., Fransen, E., Eens, M., & Stevens, J. M. G. (2015). Chimpanzee sociability is associated with vasopressin (Avpr1a) but not oxytocin receptor gene (OXTR) variation. *Hormones and Behavior*, *75*(2015), 84–90. https://doi.org/10.1016/j.yhbeh.2015.08.006;
[28] Anestis, S. F., Webster, T. H., Kamilar, J. M., Fontenot, M. B., Watts, D. P., Bradley, B. J., … Fontenot, M. B. (2014). AVPR1A Variation in Chimpanzees (Pan troglodytes): Population Differences and Association with Behavioral Style, *35*, 305–324. https://doi.org/10.1007/s10764-013-9747-z;;
[29] Gudsnuk, K., & Champagne, F. A. (2012). Epigenetic Influence of Stress and the Social Environment. *ILAR Journal*, *53*(3–4), 279–288. https://doi.org/10.1093/ilar.53.3-4.279
[30] Op cit note 29
[31] Op cit note 29
[32] To illustrate the ethical point, suppose that the study involved traumatizing the rail passenger.
[33] Hopkins, W. D., Reamer, L., Mareno, M. C., & Schapiro, S. J. (2014). Genetic basis in motor skill and hand preference for tool use in chimpanzees (Pan troglodytes). *Proceedings of the Royal Society B: Biological Sciences*, *282*(1800). https://doi.org/10.1098/rspb.2014.1223
[34] Coley, R. L., Lynch, A. D., & Kull, M. (2015). Early exposure to environmental chaos and children's physical and mental health. *Early Childhood Research Quarterly*, *32*, 94–104. https://doi.org/10.1016/j.ecresq.2015.03.001
[35] Op cit note 34

[36] Taglialatela, J. P., Russell, J. L., Schaeffer, J. A., & Hopkins, W. D. (2011). Chimpanzee vocal signaling points to a multimodal origin of human language. *PloS One*, *6*(4), e18852–e18852. https://doi.org/10.1371/journal.pone.0018852

[37] Op cit note 2, p. 62

[38]Op cit note 20.

[39] Without eliminating the variable from the experiment, there is no way to control for this confounding. There is no statistical test or randomization schedule or N that will allow a person to infer that an observed behavior is not due at least in part to the animal's confinement.

[40] Parr LA, Modi M, Siebert E, et al. (2013) Intranasal oxytocin selectively attenuates rhesus monkeys' attention to negative facial expressions. *Psychoneuroendocrinology* 38(9). England: 1748–1756. DOI: 10.1016/j.psyneuen.2013.02.011. This finding is at odds with one might expect in humans, which further undermines their use as a model. In humans oxytocin makes social cues more salient. For example, in adults with anti-social personality disorder, oxytocin increases the recognition of negative facial expressions. Timmermann M, Jeung H, Schmitt R, et al. (2017) Oxytocin improves facial emotion recognition in young adults with antisocial personality disorder. *Psychoneuroendocrinology* 85(July 2017). Elsevier: 158–164. DOI: 10.1016/j.psyneuen.2017.07.483.

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[44] Garner, J. P. (2014). The significance of meaning: Why do over 90% of behavioral neuroscience results fail to translate to humans, and what can we do to fix it? *ILAR Journal*, *55*(3), 438–456. https://doi.org/10.1093/ilar/ilu047

[45] IACUCs may allow these conditions for non-human primates, but IRBs are unlikely to allow them for human subjects research.