

# *Can a Chimp Say “No”?*

## *Reenvisioning Chimpanzee Dissent in Harmful Research*

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**Abstract:** Among the “hard cases” of captive animal research is the continued use of chimpanzees in harmful experimental science. In a recent article I contend that contemporary animal welfare science and chimpanzee behavioral studies permit, if not require, a reappraisal of the moral significance of chimpanzee dissent from participation in certain experiments. In what follows, I outline my earlier argument, provide a brief survey of some central concepts in pediatric research ethics, and use these to enrich an understanding of chimpanzee dissent useful for research ethics.

**Keywords:** animal bioethics; animal minds; chimpanzee dissent; chimpanzee research

### Introduction

Among the “hard cases” of captive animal research is the continued use of chimpanzees in harmful experimental science.<sup>1</sup> The argument for their continued use (and the option to reintroduce chimpanzees “retired” in sanctuaries) arises from such considerations as their phylogenetic proximity to humans and, so, their relevantly similar anatomical, physiological, and neurological profiles; their relevantly similar vulnerabilities to certain pathologies; and the lack of alternative animal models with a relevantly similar degree of validity.<sup>2</sup> There can be little doubt that some of these very considerations ground calls for the abolition of the same.<sup>3</sup> In drawing attention to relevantly similar moral interests reasonably thought to be shared between humans and chimpanzees,<sup>4</sup> many advocates appeal to neural structures in chimpanzees that are relevantly similar to those that underlie, among other things, pain in humans.<sup>5</sup> Indeed, the conservative nature of evolution makes it reasonable to expect a conservation of neural platforms that can underlie relevantly similar cognitive and affective capacities in chimpanzees and many humans.<sup>6</sup> Importantly, the dividing line between those opposing and those favoring the continued use of chimpanzees in harmful research does not track a substantive disagreement over chimpanzee minds.<sup>7</sup> Instead, the fundamental disagreement (and concomitant impasse) concerns chimpanzee moral status.<sup>8</sup> In moral philosophy there is wide agreement—though not unanimity—that direct duties to others are predicated on interests that arise out of the relevant individuals’ capacities to fare well or badly (or to flourish) according to their own perspective. Though I will merely assume this commitment in what follows, I am not begging a question at issue. Humane experimental science, as exemplified in William Russell and Rex Burch’s widely influential Three Rs of refinement, reduction,

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Thanks to Françoise Baylis, Ford Doolittle, audience members at a session of the 2011 Advancing Publicly Engaged Philosophy Conference in Washington, DC, reviewers for the *Cambridge Quarterly of Healthcare Ethics*, and especially Letitia Meynell, who all helped in their different ways.

and replacement,<sup>9</sup> assumes such a view when it grants that many research animals ought to be protected from excess, and/or unnecessary, pain or suffering. As this article seeks to engage the ongoing discussion to develop a consensus-building ethical framework for the scientific use of animals, my assumption reflects my primary target audience.

Neuroethics is clearly relevant to debates about invasive chimpanzee research and can facilitate discussions concerning the moral reappraisal of the use of certain nonhuman research subjects, given their historic and current importance to the neurosciences. Neuroethics can facilitate this discussion through either overtly neuro-centric frameworks<sup>10</sup> or more holistic approaches<sup>11</sup> that include insights garnered from contemporary work with animals in the relevant neurosciences when considering animal subjectivity and agency. Its relevance to debates about invasive chimpanzee research can arise from interrogating the implications of reappraising the morality of this research for the relevant neurosciences.

In a recent paper<sup>12</sup> I contend that contemporary animal welfare science and chimpanzee behavioral studies permit, if not require, a reappraisal of the moral significance of chimpanzee dissent from participation in certain experiments. In what follows, I outline my earlier argument, provide a brief survey of some central concepts in pediatric research ethics, and use these to enrich an understanding of chimpanzee dissent useful for research ethics.

### Morally Reappraising Chimpanzee Dissent

My earlier argument defending the importance of chimpanzee dissent<sup>13</sup> begins by acknowledging the growing pressure to revisit the moral status of chimpanzees, in- and outside of research. Such pressures derive not only from legislative or policy bans or restrictions on the use of great apes in captive experimental research (for more information, see the Institute of Medicine’s publication *Chimpanzees in Biomedical and Behavioral Research: Assessing the Necessity*),<sup>14</sup> but also from philosophical arguments citing relevant similarities between the interests of chimpanzees and the interests of many of those found in the human population enjoying human-level moral status. What’s more, appeals to mere species identity (that is, merely being a member of the species *Homo sapiens*) as sufficient grounds for human-level moral status have consistently failed to withstand philosophical critique. Indeed, no suggested, plausible ground for human-level moral status can be both sufficiently inclusive of those humans currently so regarded while excluding *all* of those animals used in research from which humans are excluded.<sup>15</sup>

In light of these considerations and the assumption (which arguably underlies the Three Rs framework and its use of a sliding scale of animal moral status) that some animals enjoy greater moral priority or importance than others, it is unreasonable to maintain that no nonhuman animals deserve, or should be accorded, high moral status.

Chimpanzees are the obvious candidates for human-level moral status among nonhuman animals. Moreover, their preferences are already accorded limited moral weight in contemporary animal welfare science. Importantly, ongoing studies of chimpanzee social behavior permit us to talk of the acceptability or unacceptability of the treatment of some chimpanzees by conspecifics *from the*

*perspective of* the relevant chimpanzee actors.<sup>16</sup> This can substantially enrich the conception of chimpanzee preferences that are accorded greater weight, should their moral status be elevated.

In light of the various aforementioned considerations, I conclude that their dissent can be considered a sufficient reason for excluding chimpanzees from participation in harmful scientific research.<sup>17</sup> The lack of specifications or guidelines concerning when dissent should have this effect purposefully reflects the required co-navigation of this issue involving the relevant stakeholders.

### Through the Lens of Pediatric Research Ethics

My earlier position makes much of the common currency of animal preferences in animal welfare science as well as the growing body of knowledge surrounding chimpanzee minds and sociality (including their agential capacities). In this section I indicate ways in which reexamining chimpanzee dissent through the lens of pediatric research ethics enhances the concept and elucidates the contexts of its application. Pediatric research ethics concerns research subjects who will, at least when very young, lack a sophisticated understanding of their inclusion in research, what it means to the relevant patient group(s) (or subpopulation), and what it may mean for their own well-being. As children are a vulnerable subpopulation of humans and have been historically ill-used in biomedical research, various regulations and policies have been developed to protect their interests.<sup>18</sup> Though I resist drawing strong analogies between chimpanzees (of any age) and human children as examples of incompetent research subjects, some of the concerns addressed by pediatric bioethicists mirror concerns of those working to advance discussions about the morality of harmful chimpanzee research.

In order to ensure their safe and respectful treatment in research, it is widely recognized that the willing cooperation of child subjects should be secured (both initially and, where warranted, periodically as the relevant studies continue).<sup>19</sup> How this might map onto valid consent, the capacity for which is understood as sufficient (and, for many, necessary) for decisional authority, is a matter of controversy and confusion.<sup>20</sup> The matter is further complicated by the three common categories of research: (1) research that presents minimal risk, (2) research that, though presenting greater than minimal risk, offers the potential of direct therapeutic benefit, and (3) research that, though not offering direct therapeutic benefit, presents slightly greater than minimal risk and promises to yield valuable generalizable knowledge about the relevant subpopulation.<sup>21</sup> It is disputed, for example, whether the willingness of (particularly preadolescent) children to participate in research category 1 should be a final deciding factor,<sup>22</sup> and it can be difficult to envision examples of category 2 in which the unwillingness of (particularly preadolescent) children to participate should decide the matter.<sup>23</sup>

As children present different levels of competency in making decisions affecting their fundamental interests, three basic levels of decisional capacity are discussed in the literature and variously recognized in policies and regulations.<sup>24</sup> Traditionally construed informed consent—the gold standard of ethical inclusion of human research subjects in biomedical research<sup>25</sup>—seems inappropriate for many children,<sup>26</sup> though there are those who would advocate its applicability with children aged 14 years and older (or who are otherwise mature minors).<sup>27</sup> The following point

can be exaggerated, but many children cannot achieve the understanding of a typically functioning adult about the relevant research (including *that* it is research, in contrast to therapy), the risks it poses, and the challenges they will likely encounter, as well as their right to withdraw at any time. Assent, then, is the next level of decisional capacity applied to potential child research subjects.<sup>28</sup> Challenging questions arise about how much a child must understand in order to meaningfully assent to biomedical research participation. There are those who hold that, in order to properly assent, the relevant children should be able to appreciate (in some important sense) the nature of the research, its potential benefits for other children, and the risks it poses to them.<sup>29</sup> Unsurprisingly, differing capacities for comprehension of such details among children have led to sometimes widely different approaches to seeking the cooperation of potential child research subjects. Some regard children between the ages of, roughly, 7 and 14<sup>30</sup> as capable of actively assenting to research participation, as long as the complexity of the information conveyed when seeking assent is developmentally appropriate (that is, tailored to their expected level of comprehension).<sup>31</sup>

The need for, and appropriate authority accorded to, the judgments of surrogate decisionmakers—often one or both of a child's parents—adds further complexity to this issue. Whether or not the research holds out the possibility of direct therapeutic benefit, surrogate decisionmakers are needed to protect the interests of the relevant (particularly, preadolescent) children and the expressed cooperation of such children from the undue influence of parties interested/invested in their participation.<sup>32</sup>

Already we can recognize several features of pediatric research that will not have analogues in chimpanzee research. First, appreciation of the potential benefits of this research for their peers, however impoverished or unsophisticated, requires a capacity for abstract thought that we can reasonably deny (or resist ascribing to) chimpanzees. Second, though chimpanzees show empathetic capacity when engaging with conspecifics and nonconspecifics, this should not be confused with the degree of understanding of the mental lives of others reasonably ascribed to many of those children believed to be capable of assent.<sup>33</sup> Third, the concern for the interests of chimpanzee research subjects expressed by many individuals working on animal welfare issues is not analogous to that which motivates discussions of the importance of surrogate decisionmakers in pediatric ethics. Unlike children, chimpanzees can still be profoundly harmed in institutionally and agency-approved research that lacks any direct therapeutic benefit to them. What is crucial is that the harm is intrinsic—rather than extrinsic—to the protocols or condition modeled. Extrinsic harm, or "contingent distress,"<sup>34</sup> is the target of the Three Rs efforts. Fourth, it is odd to understand the vulnerability of these chimpanzee research subjects in terms of decisional incompetence. Adult chimpanzees, and many adolescent chimpanzees, are capable of deciding, and do decide, on matters affecting their fundamental interests in free-living social contexts. That these animals do not enjoy a level of comprehension typical of properly functioning adult humans is not relevant to the question of whether the decisional capacity of adult, and many adolescent, chimpanzees is deficient or diminished. Though space limitations preclude further discussion here, elevating the moral status of chimpanzees will require careful examination of the decisional capacities of chimpanzees across their life-spans.

Returning to pediatric research ethics, it is worth noting that, though a child's capacity to assent to participation in research implies the capacity to dissent, it need

not be the case that a child capable of dissent is capable of assent.<sup>35</sup> Arguably, dissent, understood as a third level of decisional capacity, should not require a comprehension of either the potential benefits of the relevant research for others or the risks it poses to potential research subjects. Admittedly, discussions of dissent seem to conceptually link it with assent,<sup>36</sup> so this categorization of dissent as a third level of decisional capacity may be idiosyncratic. Roughly speaking, dissent understood as a third level of decisional capacity requires the following capacities: the capacity (1) for distress, pain, or stress; (2) to anticipate the future occurrence of distress, pain, or stress; and (3) to “ask” that it stop or to express that the relevant distress, pain, or stress is unwanted.<sup>37</sup> Though this understanding of dissent may be controversial, it can play an importantly different role than assent in pediatric research ethics and one much more useful to what I have in mind for captive research chimpanzees. As a complement to the judgment of a surrogate decisionmaker, the role of dissent is to minimize harm to a potential child research subject.<sup>38</sup> Just as, in animal welfare science,<sup>39</sup> the best source of knowledge for whether a research subject is undergoing unwanted distress, pain, or stress is the subject herself. For some bioethicists, a child dissenting because of (perceived) distress, pain, or stress is enough to warrant termination of his or her participation in a biomedical study.<sup>40</sup> An exception arises if the expectation of direct therapeutic benefit is sufficiently strong, if there are no viable alternative therapeutic options, and if the child research subject will not receive equally attentive care outside of the relevant research context.<sup>41</sup> It is the importance of dissent in protecting against harm arising from research that makes this construct useful for our discussion of harmful chimpanzee experimentation.

To be clear, as I note previously, I am not claiming that chimpanzees have relevantly similar capacities to those that are at work in giving either informed consent or assent in pediatric research ethics. Recalling the aforementioned conditions, what chimpanzees can do is dissent. Concerning the first capacity required for dissent, the relevant neurophysiological similarities between chimpanzees and humans strongly suggest that chimpanzees have relevantly similar capacities to humans for pain and distress.<sup>42</sup> Even when accommodating the distinctions between mere nociception and the capacity to experience the unpleasantness of pain that are common in more recent discussions of pain capacities,<sup>43</sup> chimpanzees possess, or likely possess, the relevant neurological substrates.<sup>44</sup> This inference gains considerable strength when taking into account (1) the negative behavioral responses of chimpanzees to noxious stimuli;<sup>45</sup> (2) their selective use of plants with medicinal properties when they are infected by intestinal parasites known to cause diarrhea, weakness, weight loss, and behavior that strongly suggests abdominal discomfort;<sup>46</sup> (3) the development of problematic, atypical behavior in chimpanzees that resembles symptoms of human psychological disorders in response to stimuli that, were they experienced by humans, would be traumatic;<sup>47</sup> and (4) the beneficial effect of anxiolytics in these disordered chimpanzees.<sup>48</sup> Importantly, the pain capacities of chimpanzees are not in serious dispute among those providing guidance in the use of, or those using, chimpanzees in harmful research.<sup>49</sup> Concerning the second capacity required for dissent, there is increasing evidence of capacities of chimpanzees to plan for the future.<sup>50</sup> This suggests a capacity to escape the “bounds” of the present. Coupled with what seems to be chimpanzees’ capacity for episodic-like memory<sup>51</sup> is evidence of the capacities that one might expect of animals susceptible to trauma. Anecdotal evidence that chimpanzees

are affected by memories of past pain and distress includes the stressed reaction of ex-biomedical chimpanzees, sometime after their departure from a laboratory setting, to the appearance of individuals whose clothing resembles laboratory personnel.<sup>52</sup> Concerning the third capacity required for dissent, chimpanzee sociality is especially relevant.<sup>53</sup> Opportunistic coalitions and longer-term alliances among chimpanzees in their social groups track dynamic social interactions in which the behavior of coalition or alliance members, as well as affected conspecifics, is modified over time relative to the “expressed” interests (wants or preferences) of the relevant individuals. For example, coalition or alliance members who do not reciprocate social support for another member may be punished (the unsupported chimpanzee may aggress against the offender) and may lose the future support of the relevant unsupported chimpanzee and shares in acquired resources or inclusion in social activities (e.g., shared grooming).<sup>54</sup> This capacity to modulate a conspecific’s behavior to track one’s interests (wants or preferences) evinces supporting capacities to track unwanted or undesirable behavior, the capacity to prefer a different response or set of responses, and awareness that certain behaviors can positively affect the occurrence of the desired responses from the relevant conspecifics. What appear to be tantrums of certain adult chimpanzees suggest an awareness of the failure of certain behavior-modification strategies.<sup>55</sup> The supporting capacities for these *common* expressions of chimpanzee behavior speak to the ability of chimpanzees to dissent from current (mis)treatment.

Currently, there are at least three general ways to deal with uncooperative chimpanzee biomedical research subjects: (1) tranquilize the dissenter, (2) restrain/immobilize her,<sup>56</sup> and (3) train her to cooperate through positive reinforcement.<sup>57</sup> Both methods 1 and 2 have been implicated in behavioral disorders developed by chimpanzee biomedical research subjects.<sup>58</sup> This has played an important role in motivating advocates like Balls, Goodall, and Grow to seek the end of biomedical research on chimpanzees.<sup>59</sup> Method 3 enjoys increasingly widespread support from scientists within the humane animal experimentation tradition.<sup>60</sup> Dissent offers a distinctive fourth way.

Dissent has several advantages over methods 1 through 3.<sup>61</sup> First and foremost, it maximally respects chimpanzee agency. That is to say, it not only acknowledges their agential capacities (as seen in 3 above) but also respects their expressed preference not to participate in activities that harm them (though perhaps not understood under that description). It is important to remember that this use of dissent will align this area of animal research ethics with studies of the social capacities of chimpanzees, as mentioned previously. Second, it provides an empirically tractable way of aligning chimpanzee research ethics with legislation and policy that increasingly confers special considerations on chimpanzee research subjects, while providing ways of articulating these considerations beyond vague references to genetic or behavioral similarities to humans.<sup>62</sup> Third, it nicely coheres with the recognized significance of acquiescence in a recent report from the American Institute of Medicine,<sup>63</sup> while expanding its scope beyond what the report envisions. Fourth, and not least, it answers a call in the literature to adopt standards in harmful chimpanzee research that are relevantly similar to those guiding the scientific use of human subjects.<sup>64</sup>

### Some Risks

There are risks attending the use of dissent in chimpanzee biomedical research. The most obvious is the potential failure to acquire statistically significant results

from studies in which large numbers of chimpanzee research subjects dissent from participation.<sup>65</sup> This violates the Three Rs approach of humane experimental animal science, which advocates gathering statistically significant data while doing as little harm as is necessary.<sup>66</sup> It also places at risk the chimpanzees who do not dissent and who thus participate in studies that cannot reach statistical significance.

Though real, these concerns are not relevantly different from those facing advocates of child dissent in pediatric research ethics. As long as the relevantly similar concerns do not undermine the force of this concept in the domain of child research, I see no good reason why it should here—particularly, again, as we are envisioning a context in which chimpanzees are accorded high (or higher than present) moral status.

There are two further concerns. The first has to do with the effects of distress and trauma (e.g., learned helplessness) on chimpanzees held in stressful or impoverished conditions in captivity.<sup>67</sup> The second concerns the impact of my position on the use of positive reinforcement training (PRT) to prepare chimpanzees for future laboratory experiences. Regarding the former, a learned helplessness in a population of chimpanzees could undo the moral significance of a lack of dissent in pursuing harmful research with chimpanzee subjects. This complication might encourage the introduction of surrogates into the decision process (in parallel to what we see in pediatric research ethics) in order to protect these especially vulnerable individuals, which would introduce its own complications in a context already so politically and morally loaded. After all, there is a profound danger of a conflict of interest, one that is much more profound than that which may occur in pediatric research. As noted previously, the expectation that researchers will not harm child research subjects is diminished, if not absent, in certain animal research contexts. What is more, there remains significant support for the inclusion of chimpanzees in invasive research in the relevant scientific communities that reflects the differential moral regard problematized earlier. It will also be difficult, perhaps prohibitively so, to have individuals who have no interest in the research proceeding or no biasing ties (personal or professional) to the principal investigator (or research team) stand in as surrogate decisionmakers. It has been noted that animal care staff can be effective advocates for the welfare of the research animals in their care.<sup>68</sup> Measures to minimize coercion are required before laboratory staff could play a morally decisive role in a context in which the moral status of chimpanzees has been elevated.

As to the second concern, and in light of the successes of using PRT to address many chimpanzee welfare issues in laboratories,<sup>69</sup> it would be regrettable if uptake from my position precluded the use of this training in captive settings. As the use of PRT can be reasonably understood to respect the agency of the research subjects, it need not stand in opposition to the motivations underlying my earlier arguments. Where PRT is used to manipulate the research subjects beyond initial and recurring dissent, however, it is doubtful that it is being used respectfully. Where respect for a chimpanzee's agency is the primary condition of using PRT to secure his or her voluntary participation, and short of other signs of reduced well-being (e.g., stereotypies or problem behaviors—self-mutilation, overly aggressive behavior, etc.), I defer to the subject's cooperation.

As the reader will no doubt note, what I have advocated here is not quite human-level moral status for research chimpanzees. As long as chimpanzees are involved in research that is beyond minimal risk and that does not (and is not expected to) benefit them or conspecifics, chimpanzees are not excluded from

research typically off-bounds for humans (at least those lacking a sophisticated understanding of the relevant research context). It is important to note, however, that what I am advocating moves us significantly beyond the current status quo for research chimpanzees. Indeed, in one important sense, it does involve extending human-level moral status to chimpanzees, as I am advocating a conception of dissent inspired by that which is found in pediatric research ethics.

## Conclusion

In this article I advocate the moral reappraisal of chimpanzee dissent through the lens of pediatric ethics. Though I acknowledge important relevant dissimilarities between dissent as used in pediatric research ethics and what I suggest could be used in chimpanzee research ethics, there are clear relevant similarities. Morally reappraising the dissent of chimpanzee research subjects strains, if not marks as inadequate, the current Three Rs framework, within which chimpanzee research tends to occur.<sup>70</sup> Though I have acknowledged some substantial risks and costs associated with my position, a greater risk to the moral and social legitimacy of animal experimental science arises from ignoring the agential capacities of many chimpanzee research subjects and the problematic nature of the status quo in the use of chimpanzees in harmful research.

## Notes

1. Not all chimpanzee research is harmful. See Fenton A. On the need to redress an inadequacy in animal welfare science: Toward an internally coherent framework. *Biology and Philosophy* 2012; 27:73–93.
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4. The Great Ape Project emphasizes interests in not being killed, held in captivity against their will, or subjected to torturous treatment. See Cavalieri P, Singer P, eds. *The Great Ape Project: Equality Beyond Humanity*. London: Fourth Estate Limited; 1993. Alternatively, we could talk in terms of interests not to be subjected to unnecessary pain, stress, and distress or held in conditions that cause profound problematic, atypical behaviors. See note 3, Goodall 1995.
5. See Knight A. The beginning of the end for chimpanzee experiments? *Philosophy, Ethics, and Humanities in Medicine* 2008;3(16):1–14.
6. See note 3, Goodall 1995.
7. See note 1, Fenton 2012.
8. See note 3, Balls 1995; Fenton A. Neuroscience and the problem of other animal minds: Why it may not matter so much for neuroethics. *The Monist* 2012;95(3):464–87; Hau J, Schapiro S. The welfare of non-human primates. In: Kaliste E, ed. *The Welfare of Laboratory Animals*. Dordrecht: Springer; 2007: 291–314; see note 5, Knight 2008; see note 2, VandeBerg, Zola 2005.
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12. See note 1, Fenton 2012.
13. See note 1, Fenton 2012.
14. Institute of Medicine (IOM). *Chimpanzees in Biomedical and Behavioral Research: Assessing the Necessity*. Washington, DC: The National Academies Press; 2011.
15. For references, see note 1, Fenton 2012.
16. As an example, see de Waal FBM. A century of getting to know the chimpanzee. *Nature* 2005; 437:56–9.
17. Assent and/or dissent have also been raised as possibilities for ethical consideration in the context of animal bioethics by David DeGrazia and Rebecca Walker. See DeGrazia D. Human-animal chimeras: Human dignity, moral status, and species prejudice. *Metaphilosophy* 2007;38(2–3):309–29; Walker RL. Human and animal subjects of research: The moral significance of respect versus welfare. *Theoretical Medicine and Bioethics* 2006;27:305–31. Though we are clearly in agreement on the power of assent and/or dissent, my resistance to using personhood distinguishes my argument from DeGrazia's, whereas my *detailed* use of pediatric research ethics in this article to inspire my account of dissent distinguishes my position from both DeGrazia's and Walker's.
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21. See note 18, Diekema 2006.
22. Baylis F, Downie J. The limits of altruism and arbitrary age limits. *American Journal of Bioethics* 2003;3(4):19–21; see note 20, Baylis et al. 1999; see note 18, Diekema 2006.
23. See note 20, Baylis et al. 1999; see note 18, Diekema 2006; see note 20, Kon 2006.
24. See note 20, Kon 2006; Miller VA, Drotar D, Kodish E. Children's competence for assent and consent: A review of empirical findings. *Ethics and Behavior* 2004;14(3):255–95.
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26. See note 18, Diekema 2006.
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33. See Brosnan S. Inequity and prosocial behavior in chimpanzees. In: Lonsdorf EV, Ross SR, Matsuzawa T, eds. *The Mind of the Chimpanzee: Ecological and Experimental Perspectives*. Chicago: The University of Chicago Press; 2010:282–95; de Waal FBM. Putting the altruism back into altruism: The evolution of empathy. *Annual Review of Psychology* 2008;59:279–300.
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36. For examples, see note 20, Baylis et al. 1999 and Kon 2006; Leikin S. Minors' assent, consent, or dissent to medical research. *IRB: Ethics and Human Research* 1993;15(2):1–7; see note 30, Meaux, Bell 2001.
37. See note 18, Diekema 2006.
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48. See note 47, Brüne et al. 2006.
49. See note 43, CRAPLA 2009; see note 14, IOM 2011.
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51. Martin-Odas G, Haun D, Colmenares F, Call J. Keeping track of time: Evidence for episodic-like memory in great apes. *Animal Cognition* 2010;13:331–40.
52. I was visiting a sanctuary for ex-biomedical chimpanzees when some other visitors elicited this reaction.
53. See note 1, Fenton 2012.
54. See note 33, Brosnan 2010; see note 16, de Waal 2005.
55. See note 33, Brosnan 2010; Menzel EW. A group of young chimpanzees in a 1-acre field: Leadership and communication. In: Byrne R, Whiten A, eds. *Machiavellian Intelligence: Social Expertise and the Evolution of Intellect in Monkeys, Apes, and Humans*. New York: Clarendon Press; 1988:155–9.
56. See note 34, Bloomsmith, Else 2005; Laule G. Positive reinforcement training for laboratory animals. In: Hubrecht R, Kirkwood J, eds. *The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals*. 8th ed. West Sussex, UK: Blackwell; 2010:206–18.
57. See note 45, Perlman et al. 2010.
58. See note 45, Bradshaw et al. 2008.
59. See note 3, Balls 1995; see note 3, Goodall 1995; see note 45, Bradshaw et al. 2008.
60. See note 34, Bloomsmith, Else 2005; see note 56, Laule 2010; see note 45, Perlman et al. 2010.
61. The discussions in DeGrazia and Walker are helpful here. See note 17.
62. See note 14, IOM 2011; see note 5, Knight 2008.
63. See note 14, IOM 2011.
64. Gagneux P, Moore JJ, Varki A. The ethics of research on great apes. *Nature* 2005;437:27–9; see note 3, de Waal 2012.
65. I noted this problem in my previous article. See note 1, Fenton 2012.
66. Schuppli CA, Fraser D, McDonald M. Expanding the Three Rs to meet new challenges in humane animal experimentation. *Alternatives to Laboratory Animals* 2004;32:525–32.
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68. Nelson RJ, Mandrell TD. Enrichment and nonhuman primates: “First, do no harm.” *ILAR Journal* 2005;46(2):171–7.
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