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Humanity and Inhumanity of Nonhuman Primate Research

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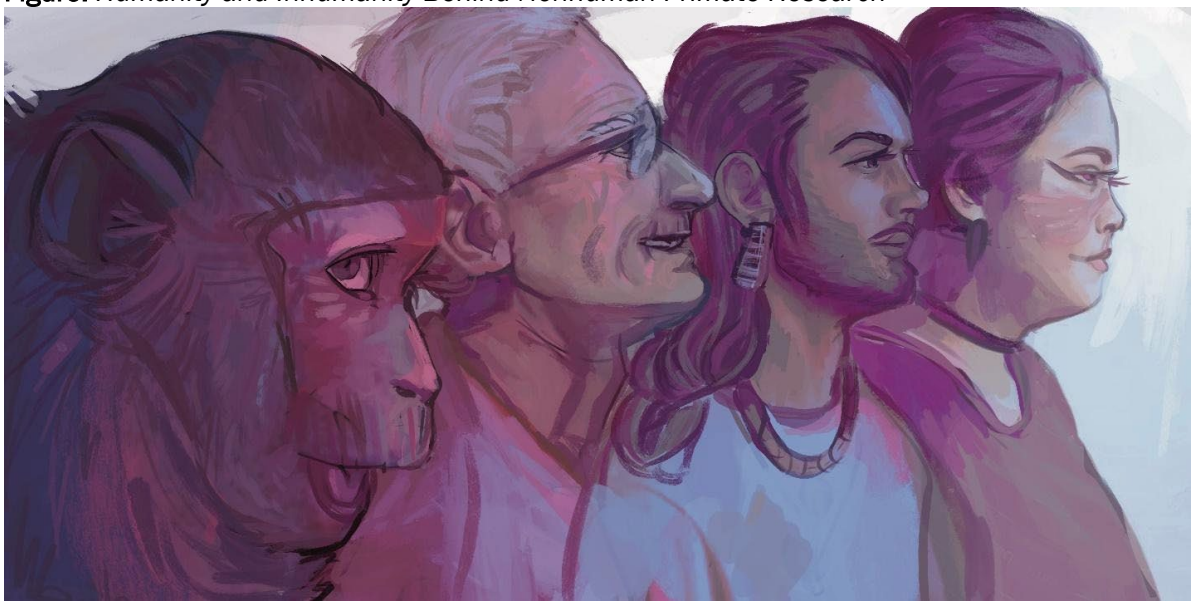
Abstract

This illustration depicts important biomedical advancements generated by nonhuman primate (NHP) research. NHPs' value in human-centered research is their unique evolutionary proximity to humans.

Primates in Human-Centered Health Research

Despite public hostility, nonhuman primate (NHP) research has contributed invaluable knowledge about disease states and drug therapies that have benefited underserved human communities.[1] This success further complicates ethical conversations about uses of NHPs[1,2]; the illustration represents a spectrum of human interest by visually elucidating interrelations among NHP research and advancements in human-centered health.

Figure. *Humanity and Inhumanity Behind Nonhuman Primate Research*



Media

iPad, Procreate.

NHP research has triggered widespread public outrage and activism. Notable instances include the infamous "pit of despair" experiment conducted by comparative psychologist Harry Harlow, which horrified the public by putting young rhesus macaques under extreme psychological distress.[3,4,5] A doctoral student of Harlow, Gene Sackett, said animal rights advocates' hatred was so intense that he personally believed it was Harlow and his experiment that started the modern animal rights movement.[3] In the 1980s, Edward Taub's Silver Spring monkeys sparked allegations of limb deafferentation, improper housing conditions, and poor veterinary care.[3] Taub had been using NHP deafferentation experiments to test his hypothesis of learned non-use and its applications to human stroke rehabilitation, which facilitated development of constraint-induced movement therapy.[3,6] NHP researchers have also been the target of attacks by animal rights groups, such as a string of attacks on California NHP researchers in the mid-to-late 2000s.[4] More recently, in 2020, the University of Wisconsin-Madison was fined $74 000 by the US Department of Agriculture for 28 violations of federal animal research standards, such as injuries requiring amputations.[7]

Human Interest Illustration

One subject, at left in the illustration, is the rhesus macaque, 1 of 2 preferred species in NHP research and the same species used in Harlow's experiments.[3] Each person to the right in the illustration represents the impact of NHP-derived medication on one particular difficult-to-treat or understudied human disease. The first subject, an older man, symbolizes the impact of new treatments for neurodegenerative diseases, such as Parkinson's (PD) and Alzheimer's disease (AD), on length and quality of life. NHP models for PD became critical after the discovery of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).[8] After "identifying MPTP as the likely cause of permanent parkinsonism,"[8] early studies using MPTP with NHP models for PD emerged. NHP models gained prominence at this moment, as traditional rodent models showed moderate-to-severe resistance to neurotoxic effects of MPTP.[9,10] Even today, NHP models for PD help improve cell-based treatments[11] and serve as critical models for early-stage tau pathology in AD. (Rodents have little tau pathology, and early-stage tau phosphorylation is difficult to study in humans postmortem.[12])

The second human subject in the drawing, a young queer man, represents the impact that HIV/AIDS medication development has had on gay communities and survivorship. The extensive contributions of NHP research to HIV/AIDS treatment include evaluation of Tenofovir's toxicity and its efficacy in suppressing viral replication and testing its prophylactic use as early as 1996.[13]

The last person in the illustration has a malar rash, one of the most well-known symptoms of systemic lupus erythematosus (SLE), and represents the impact of new treatments for SLE on quality of life.[14] NHP models were critical in advancing SLE care: cynomolgus monkeys were used for toxicity testing and dosage testing of the biologic belimumab.[15] Before the US Food and Drug Administration approved belimumab in 2011, no new drug treatment specifically targeting SLE had been released in 56 years, and treatment options up to that point were often inadequate.[15]

References

1. Friedman H, Ator N, Haigwood N, et al. The critical role of nonhuman primates in medical research. *Pathog Immun*. 2017;2(3):352-365.
2. Working Party on the Ethics of Research Involving Animals. *The Ethics of Research Involving Animals*. Nuffield Council on Bioethics; 2005. Accessed May

4, 2024. https://www.nuffieldbioethics.org/assets/pdfs/The-ethics-of-research-involving-animals-full-report.pdf
3. Blum D. *The Monkey Wars*. Oxford University Press; 1996.
4. Pushing the limits. Editorial. *Nat Immunol*. 2008;9(5):445.
5. van Rosmalen L, Luijk MPCM, van der Horst FCP. Harry Harlow's pit of despair: depression in monkeys and men. *J Hist Behav Sci*. 2022;58(2):204-222.
6. Taub E. The behavior-analytic origins of constraint-induced movement therapy: an example of behavioral neurorehabilitation. *Behav Anal*. 2012;35(2):155-178.
7. Meyerhoffer K. UW-Madison fined $74,000 over care of research animals. *Wisconsin State Journal*. July 30, 2020. Accessed May 4, 2024. https://madison.com/news/local/education/university/uw-madison-fined-74-000-over-care-of-research-animals/article_4dc49f41-7b27-5291-bff6-b95096d71d9e.html
8. Langston JW. The MPTP story. *J Parkinsons Dis*. 2017;7(suppl 1):S11-S19.
9. Burns RS, Markey SP, Phillips JM, Chiueh CC. The neurotoxicity of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in the monkey and man. *Can J Neurol Sci*. 1984;11(1)(suppl):166-168.
10. Johannessen JN, Chiueh CC, Burns RS, Markey SP. Differences in the metabolism of MPTP in the rodent and primate parallel differences in sensitivity to its neurotoxic effects. *Life Sci*. 1985;36(3):219-224.
11. Vermilyea SC, Emborg ME. The role of nonhuman primate models in the development of cell-based therapies for Parkinson's disease. *J Neural Transm (Vienna)*. 2018;125(3):365-384.
12. Arnsten AFT, Datta D, Preuss TM. Studies of aging nonhuman primates illuminate the etiology of early-stage Alzheimer's-like neuropathology: an evolutionary perspective. *Am J Primatol*. 2021;83(11):e23254.
13. Hammack PL, Toolis EE, Wilson BDM, Clark RC, Frost DM. Making meaning of the impact of pre-exposure prophylaxis (PrEP) on public health and sexual culture: narratives of three generations of gay and bisexual men. *Arch Sex Behav*. 2019;48(4):1041-1058.
14. Naji Rad S, Vashisht P. Malar rash. In: *StatPearls*. StatPearls Publishing; 2024. Accessed July 24, 2024. https://www.ncbi.nlm.nih.gov/books/NBK555981/?report=reader
15. Dubey AK, Handu SS, Dubey S, Sharma P, Sharma KK, Ahmed QM. Belimumab: first targeted biological treatment for systemic lupus erythematosus. *J Pharmacol Pharmacother*. 2011;2(4):317-319.

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