



What can caged lab monkeys tell us about free human beings?

Where biomedicine gets it wrong about primate research.

by **Garet Lahvis**

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A macaque sits in a cage in a University of Muenster laboratory in Muenster, Germany, on November 24, 2017. Friso Gentsch/picture alliance via Getty Images

A friend says they can always tell when you're hungover. The way you close the cage latch. With so little to do, their attention can focus on those subtle differences in movement: the way it turns, whether it drops all or part of the way.

After easing the latch back open, the monkey climbs down to the concrete floor, past the rolling service station with its cotton swabs, boxes, bottles, and syringes.

Out in the hallway, two caretakers see him crouched against the cinderblock wall, hands pressed against the cream-colored paint, shoulders pulled up, head turned sideways and facing down the corridor, eyes toward them.

Over the past couple of years, experimentation on non-human primates has had a run of bad publicity. In 2020, media attention focused on a federal laboratory that studied the neurobiology of anxiety by scaring monkeys with toy snakes. In November, the US Justice Department indicted members of an alleged “primate smuggling ring” for trafficking and selling wild long-tailed macaques, an endangered species, to biomedical researchers in the US.

Around the same time, attention turned to the Livingstone Lab at Harvard University, where researchers sewed baby macaques’ eyelids shut to investigate how visual deprivation affects brain development. The controversy landed in Science magazine, where scientists debated the ethics of blinding monkeys. I was asked to weigh in. But my questions were different — less about the blinded macaques, and more about the controls staring at their cage walls.

For 16 years, I worked as a professor for medical schools in Wisconsin and Oregon. Both universities had primate centers. I knew about their operations, though I never experimented on primates. Instead, my laboratories mostly studied mice. Our goal was to identify the genetic and pollutant risk factors for autism, a disability that features challenges with social emotions. We never successfully identified any risk factors, but we did discover that mice enjoy one another’s company and have empathy for their pain.



After publishing more than 40 scientific papers, I left academia. In part, I left on principle. I believed that if we experimented on animals, we were obligated not to waste them. I also believed that biomedical scientists were obliged to consider the implications of our own discoveries — like how our animals were responding to their cage environments — so we could do better science. Eventually, I lost faith in the process. I also lost the stomach to confine sentient creatures to tiny cages.

Scientists know that the tight confinement of standard laboratory cages distorts the psychology and physiology of our animal subjects. Yet despite a half-century of evidence, we continue to cage them as if their biology is baked into their genetics. From decades of rodent studies, scientists know that an animal's brain anatomy and physiology are highly vulnerable to even modest changes in their living environments. Mice housed in standard cages, rather than slightly larger ones furnished with blocks and tunnels for mental stimulation, are more susceptible to drug abuse, genetic modifications, and toxic chemicals. Monkeys, nearly our next of kin, can become so mentally deranged by their cage environments that they no longer resemble healthy humans. They might have more in common with children housed in Romanian orphanages in the 1980s and 1990s, who were so deprived of human contact that they still struggle with lifelong physiological and psychological disabilities.

Can we use mentally damaged animals to model mental health?

Primate experiments have undeniably aided the discovery of treatments for human disease, particularly vaccines and surgical techniques. More than a century ago, for example, scientists collected extracts from the spinal cord of a boy who died of polio, injected them into monkeys, studied how the infection spread, and then developed a vaccine that nearly eradicated polio. Much more recently, primate experiments were useful for developing a brain-spine interface that can restore the ability of people with paralysis to walk.

But these successes have been rare. Part of the problem lies in the question we now ask. Globally, scientists use approximately 100,000 non-human primates at any given time, often to explore highly nuanced questions, like finding risk factors and treatments for mental health challenges — autism, ADHD, schizophrenia, addiction, anxiety, depression, post-traumatic stress disorder. And here, we mostly fail. Most drugs showing extreme promise in animal studies fall short in human trials. We haven't developed a new category of drugs for treating psychiatric illness in more than 50 years; new psychiatric drugs introduced over the same period have been modified versions of existing drugs.

Scientists also use primates to understand how human-like immune systems respond to infectious diseases — but, like mental health, immunity is also highly sensitive to how the monkeys feel inside their cages.

Housing for monkeys is tight. The standard cage for a rhesus macaque, a common laboratory primate, is about 2.5 feet across, narrow enough for its inhabitant to touch both walls at once. By contrast, their wild relatives can navigate home ranges averaging about 1.5 square miles. Macaques are built to navigate 740 American football fields' worth of savannah grasslands and forest canopies. Yet inside biomedical labs, they typically get confined to the equivalent of a telephone booth.

Housing situations vary. Some live “singly housed” — a situation that resembles solitary confinement, often for a few months, sometimes for life. Others get “protected contact” — two monkeys separated by a grate that permits fingertips to touch. Others

live as “buddies in a cage” — sharing the space of a shower stall until one buddy gets pulled out, often leaving the remaining one stressed and with a depressed immune system for weeks to months depending on his temperament (and, perhaps, how close he felt to his buddy).

In some respects, singly housed monkeys have it better than human inmates in solitary. For instance, they can more easily hear each other vocalize. Some have handheld mirrors to see their neighbors. Many have opportunities to rattle their squeeze bars, the metal poles fixed to the cage’s back walls, used to pull the monkeys forward for procedures like injections and blood draws. But while the United Nations considers more than 15 days of solitary confinement in humans to be torture, research monkeys often get a lifetime — especially if they lose it and assault their buddy in the cage. And although humans in solitary get time each day outside their cell, primates usually don’t get a break.

Studies show that human solitary confinement in prisons can cause depression, anxiety, paranoia, violent fantasies, full-blown panic attacks, hallucinations, psychosis, and schizophrenia. Some incarcerated people also self-mutilate, cutting their wrists and arms, ingesting foreign objects, self-burning, and reopening stitches from prior injuries. Physical symptoms include cardiovascular disease, migraine headaches, back pain, profound fatigue, and deterioration of eyesight.

Likewise, lab monkeys express behaviors that suggest psychological trauma. Among 362 singly housed rhesus monkeys, a study found that 89 percent expressed abnormal behavior. Most were what we call “stereotypies” — repetitive behaviors that serve no purpose, save coping. Some monkeys pace in circles. Others rock or bounce for hours, like idling engines. Some methodically somersault. Others incessantly rattle their squeeze bars. A few spend time in “eye salute,” a euphemism for self-stimulation by sticking fingers into one’s own eye.

My friend tells me he’s seen some monkeys cross the line of no return. Unresponsive to the caretakers interacting with them, they can’t stop rocking, twirling, circling, or

twitching. They can't pull away from the back of the cage. Their eyes no longer make contact.

Up to 15 percent of laboratory monkeys self-mutilate. They might pluck single hairs from their backsides until they turn bright pink, or bang their heads repeatedly against their cage walls, or bite themselves deep enough to require sutures. Unlike their wild brethren, caged macaques often paint the walls with their feces — a substance they can manipulate.

Nearly one-quarter of caged macaques express “floating limb” behaviors. Watch one for long enough and you might see his leg writhe or kick. He might grab his leg as it slowly elevates, seemingly out of control. It might hover behind his back. Or his foot might relentlessly smack the back of his head. He might respond by attacking his leg, as if it were foreign.

Scientists have normalized the idea that their caged primates are healthy

I suspect these behaviors are manifestations of an intolerable allostatic load: a “wear and tear on the body and brain resulting from chronic overactivity or inactivity of physiological systems that are normally involved in adaptation to environmental challenge.” Cramped living spaces deny primates the ability to act on their innate motivations: to seek pleasures, avoid discomforts, and explore complex and changing environments. Oysters don't need these motivations because they can flourish cemented to a rock. For moving animals, motivations help us make decisions. An innate taste for sugar and salt prompts us to seek the calories and sodium we need to survive. When scientists remove the pleasure center of a rat brain, called the nucleus accumbens, they no longer eat.

Curiosity is also an innate drive. In the wild, animals feel compelled to investigate their environments — where to go, what to eat, with whom to interact — to know their options when their situations change. Scientists leverage an animal's innate curiosity to study how memory works: Introduce a laboratory mouse to a novel object and a

familiar one, and if the rodent remembers the object they encountered before, they'll spend more time sniffing the unfamiliar one. Since the 1950s, scientists have known that monkeys will solve complex puzzles simply for the challenge of solving the task.

I suspect that, deprived of varied and ongoing challenges to overcome, environments to explore, or a natural range of body movements, caged monkeys — studied because they resemble us — go insane with boredom. Still, I've heard scientists insist that these animals are happier in cages because they get food, water, and safety from predators. They'll tell you laboratory primates get “environmental enrichment,” like a rubber ball stuffed with a treat, a toy dangling from a cage door, a mirror to play with, or snacks scattered on the cage floor. I suppose they get exercise, too. For glutes and biceps, they can rock back and forth or rattle their cage doors. For a cardio workout, they can pace in circles or slam themselves against the cage walls.

Here's the rub. Scientists must believe that lab animals thrive physically and mentally — not for animal welfare reasons, but to justify our experiments. We need healthy controls, not psychologically broken ones, to benchmark our disease models. And we need the animals used as disease models to be otherwise healthy because we lack the scientific capacity to separate the biology of a nuanced disorder, like autism or ADHD, from confounding factors like the mental damage caused by incarceration.

My qualm with the Livingstone Lab's experiment, the one that entailed sewing baby monkeys' eyelids shut, is not primarily ethical but scientific. They claimed that by blinding monkeys, they could gain “insight into evolutionary changes in the functional organization of high-level visual cortex.” But they wrongly presumed that their “healthy” control monkeys, who were denied most visual stimulation save the depleted sensory environment of a steel-gray cage, had normal visual functioning.

By describing what they're studying as “evolutionary changes,” the researchers lured us into believing the ridiculous — that brain development behind steel bars is not only normal but natural enough to be relevant to evolutionary changes occurring outside the lab. Yet their monkeys experienced no full spectrum of color, no natural movement like the rustling of leaves, and no passing landscape. Like most other primate experimenters, the lab normalized the idea that monkeys naturally live inside

telephone booths, not in the vast, dynamic, and aesthetically complex expanses of nature.

What bothers me most is that the scientific community expresses so little concern about whether we're chasing artifacts of confinement. And for the few of us who ask, the answer is loud with silence.

Can we do better?

Admittedly, scientists are in a fix. Our problem might have begun during the late Middle Ages, about 800 years ago, when Italian philosopher and theologian Thomas Aquinas argued that because animals lacked “rational souls,” they were like machines. Centuries later, René Descartes, a father of modern science, called animals *automata*, robots driven by reflexes, without thoughts or feelings — like the mechanical men of his era, built to hammer the bells of village clock towers. Armed with this philosophy, scientists tacked dogs to walls and opened them up without anesthesia to learn that the heart, not the liver, pumped blood. Their shrieks and howls were thought of as if they were bells ringing on the hour.

The cruel irony is that the ethical justification for experimenting on animals — that they lack subjective experiences — allowed us to find cogent evidence that they do. Now we're forced to ignore what we've learned from science — so that we can keep doing it.

Rather than envision a new paradigm, scientists have devised arguments to keep things the same, claiming, for example, that we need small cages to control for confounding variables in an animal's environment. But we routinely accept the inescapable variables inside their confines — sound, lighting, food quality, social situations — that are either impossible or too inconvenient to control. In truth, we use small cages because they afford the cheapest and most convenient way to generate scientific publications.

What could scientists do differently? We could pivot to more helpful alternatives. We could deploy spatially and temporally complex spaces to study smaller organisms under conditions where they might thrive like the free human beings they are meant to resemble. Mice and rats could live in small research barns with varied food and shelter

options and penned-in outdoor access, where they could author their own experiences and meet ongoing and unpredictable challenges. Zebrafish, snails, and fruit flies could also get environments complex enough to operate as they might in the wild. Remote technologies could help deliver various drugs and biomolecules to moving animals and help us monitor their responses.

Biomedical research institutions could double down on financially neglected health research programs, like disease prevention. We could expand monitoring of human and wildlife populations for elevated pockets of disease — like cancer, congenital disorders, and mental illness — arising from our exposures to thousands of pesticides and industrial contaminants.

Present-day concerns over “forever chemicals” in our food and drinking water, and the enormous price tag we now face for cleanup, could have been predicted and more easily remediated decades ago, when epidemiologists and chemists found evidence of their presence in humans and wildlife. The elevated prevalence of congenital disorders, endocrine disruption, immune dysfunction, and mental illness found in fish-eating wildlife in pollutant hot spots around the Great Lakes and along the US coasts could be used to identify regional exposures to chemical mixtures that also threaten human health. Why not focus on these issues? With advanced epidemiological computer modeling, and gene sequencing tools, along with high-efficiency cell culture systems that can test multiple chemicals at a time without the use of animals, we could identify harmful compounds, then remove them. The potential is far greater than whatever we might learn from using rubber snakes to scare mentally enfeebled monkeys.

Many people believe that science differs from blind faith. If that’s true, I wonder how many more rabbit holes we’ll plumb before we see that cage-deteriorated primates don’t resemble free human beings. Perhaps scientists collectively disregard animal subjectivity out of fear of the moral implications of experimenting on other sentient creatures. Or are we blinded by our ambitions for careers and legacies? No matter the cause, we have obligations to the societal trust placed in us. And if we’re 1,000 years overdue for a paradigm shift, let’s hope that today’s young scientists can find the unfettered clarity of sight to make it happen.

The fugitive still cowers in the main hall, cheek and chest pressed against the cinderblock, eyes looking upward, seemingly fixed on the audible ballast of the fluorescent lights. Or the fly circling, then resting, beneath it. He might hear the buzz of both, one against the other, a two-tone that cannot calm the anxiety of being outside that room. Having known only metal walls and the fetid mire of idling bodies, he lacks familiarity with concrete surfaces, unfouled air, and the taking of risks.

The protocol is straightforward. Face the escapee, chest out, shoulders straight, eyes toward his. Wedge open the colony room door. Use push brooms to coax him back into his cage.

The convict returns. They close his cage door. He pivots, then grabs the bars of the door as if he's now the master, then shakes them violently like he's trying to get out. He'll be studied over and over again because he somehow represents us. Maybe he does.

Garet Lahvis was an associate professor and the graduate program director of behavioral neuroscience at Oregon Health and Science University. He is currently writing a book for the University of Chicago Press on his experiences with the limits of science, and of the scientific community, in addressing some of our most pressing biomedical issues. Follow him on X (formerly Twitter) at @GLahvis.

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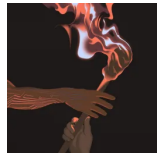
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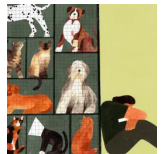


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