Review of Neuropsychology Experiments on Rhesus Macaques at the National Institutes of Health

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‘Mental Illness’ Experiments on Primates at the National Institutes of Health: An Executive Summary

For more than 30 years, National Institutes of Health (NIH) investigator Elisabeth A. Murray has been inflicting permanent, debilitating brain damage on rhesus macaques and conducting painful, frightening, and unnecessary experiments on them. The experiments have cost U.S. taxpayers nearly $49 million since 1998 and have not resulted in any new treatments or cures for human mental illness. NIH needs to stop supporting these archaic experiments and close this laboratory.

These experiments cause extreme harm to sensitive, vulnerable monkeys.

- Young monkeys in this laboratory are subjected to numerous invasive surgical procedures, including the following:
  - Experimenters cut into the animals’ heads, remove a portion of their skulls, and inject toxins into their brains to kill off large areas of brain tissue.
  - They then surgically and permanently affix objects called “head posts” directly into the monkeys’ skulls. These are used to force the animals to hold their heads completely still for hours at a time.
  - Experimenters also cut permanent holes into the primates’ skulls so that they can inject drugs directly into their brains.

- Monkeys in this laboratory are forced to endure fear- and stress-inducing living conditions and experimental procedures, including the following:
  - Experimenters place them alone in small, dark cages and then deliberately terrify them with fake but realistic-looking snakes and spiders, which they innately fear.
  - Experimenters restrain the monkeys for hours at a time, startle them with puffs of air blown directly into their eyes, force them to drink bitter-tasting liquids, and deprive them of food and water to compel them to “cooperate.”
  - Experimenters also deprive these animals of social interactions with their peers, which causes them severe physiological and physical damage, including hair loss, systemic inflammation, and self-injurious behavior.

- After enduring years of captivity, social isolation, painful surgeries, and terrifying experimental procedures, these monkeys are killed and dissected.

These experiments are scientifically meaningless, unnecessary, and inapplicable to humans with mental illness.

- Captivity induces negative effects in primates, causing numerous confounding physiological and psychological health issues that make data from this laboratory worthless.
- Humans with mental illness do not have brain damage similar to what is being caused in this laboratory.
- The behavioral tasks used in this laboratory do not measure the types of complex behavior typically problematic for individuals with mental-health conditions.
- Numerous humane, clinically relevant research methods are available for studying the underlying causes of mental illness in humans.
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For more than 30 years, Elisabeth Murray, an investigator at a National Institute of Mental Health laboratory in the Intramural Research Program, has been inflicting permanent brain damage on rhesus macaques via aspiration (suctioning out brain tissue) or excitotoxic lesions (cell death caused by the injection of toxins) and then studying their response to threatening or aversive stimuli. The purported aim of these experiments is to clarify the roles of different brain regions in behavioral flexibility, reward processing, and social behavior and to apply the findings to humans with neuropsychiatric illness.

As will be demonstrated below, we believe these experiments are ethically and scientifically unjustifiable given the considerable harms inflicted on the monkeys involved, the limited applicability of the results to humans and human illness, the lack of benefits produced for humans or animals, the financial costs, and the numerous alternative research methods available.

Harms

Murray inflicts permanent brain damage in monkeys by subjecting them to craniotomies (cutting into and removing part of the skull to expose the brain) and performing intracranial injections of excitotoxins (compounds that may cause injury to nerve cells). These injections can cause tachycardia (rapid heart rate) or respiratory arrest, which may take between 30 minutes and five hours to resolve. Monkeys used in the laboratory’s “disconnection” experiments undergo two or three separate invasive surgeries to lesion different parts of the brain in stages. Additional surgeries are sometimes required to repair misplaced or incomplete lesions.

Many monkeys undergo an additional surgery in which head posts are affixed to the top of their skulls with screws and cement. It takes up to four weeks for them to heal from this surgery, and some of them end up living with these posts attached to their skulls for years. After recovering from head-post surgeries, many monkeys undergo yet another major surgery, in which holes are cut for chambers to be placed in their skulls so that experimenters can inject pharmaceutical compounds directly into their brains. In some instances, experimenters accidentally hit a blood vessel, resulting in brain hemorrhaging. Additional surgeries are sometimes required in order to scrape away bone that has grown into the chambers.
The behavioral deficits caused by many of the lesions that Murray inflicts impair the monkeys’ ability to engage normally with conspecifics (other monkeys), so many of the animals in this laboratory are forced to live in isolation. Social isolation causes primates severe physiological and psychological harm and frequently leads to the development of abnormal and self-injurious behavior patterns, including hair-plucking, hair-pulling, biting, digit-sucking, eye-poking, self-clasping, and other forms of self-mutilation that can lead to significant injury and morbidity.1

In some experiments, monkeys are deliberately terrified with realistic-looking rubber snakes and spiders as well as the fear-inducing “Human Intruder Test,” in which an unfamiliar, apparently threatening human approaches and stares at the monkeys. In other experiments, Murray and her laboratory staff blow puffs of air into the monkeys’ eyes or deprive them of water to make them thirsty enough to drink bitter-tasting liquids like citric acid and quinine so that experimenters can see how they react to aversive stimuli. For many experiments, the monkeys are forced to wear a metal or hard-plastic collar and are strapped into a restraint chair that keeps their heads, arms, and legs immobilized. Monkeys in this laboratory are also required to lie awake with their bodies and heads restrained in a magnetic resonance imaging (MRI) scanner for up to five hours at a time.

Rhesus macaques, like all primates, are highly intelligent, complex, social animals who endure extreme physiological and psychological harm when held captive in laboratories. Pacing, rocking, head-twisting, biting their own flesh, and pulling out their own hair are just some examples of the stress-related behavior exhibited by primates in laboratories.2,3,4,5 They also suffer from various immune system abnormalities, including increased stress hormone levels, dysregulation of the hypothalamic-pituitary-adrenal axis, and immune system depression.6 This stress-induced immune dysfunction often leads to increased vulnerability to infection,7 chronic autoimmune disease,8 delayed wound healing, delayed recovery from surgeries,9 and accelerated aging.10

**Scientific Limitations**

The experimenters justify the extremely harmful procedures described above with the argument that they will provide a better understanding of the neural underpinnings of neuropsychiatric illness. However, there are numerous limitations to these experiments that make the likelihood of these data being meaningfully applicable to humans extremely low.

Decades of research with patients have taught us that the brain abnormalities associated with most neuropsychiatric illnesses are not comparable to the type of brain damage inflicted on monkeys in this laboratory. Neuropsychiatric patients have very subtle anatomical
abnormalities not usually detectable by standard imaging methods.\textsuperscript{11,12,13} Moreover, there are fundamental species differences in gene expression and protein function,\textsuperscript{14} immune system functioning,\textsuperscript{15} neurodevelopment,\textsuperscript{16,17} neuroanatomy,\textsuperscript{18,19} age-related changes in hormone production,\textsuperscript{20} and age-related neurodegeneration.\textsuperscript{21,22}

The rearing history of these monkeys (whether they were raised by their mothers or in a nursery and whether they were born in a laboratory or in nature) is also variable, despite the wealth of data indicating that rearing conditions have a profound impact on primates’ brain development as well as their social, cognitive, and physical well-being.\textsuperscript{23,24,25} Additionally, the monkeys in this laboratory are of a variety of ages at the time the lesions are inflicted, even though the age at lesion onset is known to have an impact on the type and degree of behavioral impairments experienced by humans.\textsuperscript{26,27,28,29,30,31} Many of the monkeys are obtained from the National Institutes of Health nonhuman primate “recycling” program, indicating that they have previously undergone experimental procedures, which may have been harmful and could certainly introduce confounding variables.

**Non-Animal Alternatives**

There are several alternative research methods available for studying the neural correlates of behavior (brain activity that corresponds with and is necessary to produce a particular experience) in healthy and clinical human populations. Researchers have been studying the roles of specific brain regions for emotional regulation,\textsuperscript{32,33} behavioral flexibility,\textsuperscript{34,35,36} and reward processing\textsuperscript{37,38} in humans for decades.

Researchers studying patients with naturally occurring focal lesions\textsuperscript{39,40,41} (injury to limited areas of brain tissue) and using transcranial magnetic stimulation to study the effects of temporarily disabling regions of the brain safely\textsuperscript{42} have successfully determined the role of different brain regions in the behavior types being studied in Murray’s laboratory. These tools have been used to study brain structure and function in neuropsychiatric patient groups that exhibit difficulties with the types of behavior that she is trying to measure in monkeys.\textsuperscript{43,44,45}

Additionally, postmortem analysis of brain tissue from patients\textsuperscript{46,47,48,49} and large-scale epidemiological studies\textsuperscript{50,51} are also helping researchers understand the neurobiological underpinnings\textsuperscript{52,53} and the complex genetic and environmental factors that contribute to neuropsychiatric illness.\textsuperscript{54}

**Conclusion**

These experiments, which inflict considerable harms upon primates, have extremely limited potential to elucidate the complex etiology (the cause or origin of a disease) of human mental illnesses and have not yet improved our treatment of these conditions or otherwise advanced human health in any measurable way. Continuing these projects represents an enormous financial burden on taxpayers and is particularly wasteful given that there are readily accessible, humane research methodologies available for obtaining data that are applicable to human mental illness and its treatment. Murray’s experiments on monkeys are not scientifically or ethically justifiable.
Endnotes


