Citizens for Alternatives to Animals Research & Experimentation
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July 13, 2022

Dear Mr. Ford,

I am writing on behalf of Citizens for Alternatives to Animal Research and Experimentation (CAARE), a national nonprofit dedicated to promoting research that does not use animals. This letter expresses the opinion of our board, staff, consultants, and tens of thousands of supporters.

We were very disturbed to learn about invasive brain experiments on monkeys carried out in the Laboratory of Neural Systems at Rockefeller University. We believe that in the first quarter of the twenty-first century experiments like this are demonstrably outdated and unjustifiable.

As one of the world's most prestigious research universities, with a stated "singular focus on powering the breakthroughs that will transform medicine" such a heavy emphasis on translational research from monkeys does not scientifically support Rockefeller University's mission.

There is mounting and undeniable evidence that animal experiments translate poorly to human biology. [1] [2] [3] [4] Moreover, scientists today have at their disposal a wide range of sophisticated, human-relevant means for studying the human brain.

For example, scientists at Carnegie Mellon University carried out ethical research with human volunteers to study how the brain processes facial recognition, similar to the project carried out on monkeys in the Rockefeller laboratory of Winrich Freiwald.

To determine how the brain rapidly distinguishes faces, the Carnegie Mellon team scanned the brains of four people using non-invasive magnetoencephalography (MEG). MEG allowed them to measure ongoing activity throughout the brain on a millisecond-by-millisecond basis while the participants viewed images of 91 different individuals with two facial expressions each: happy and neutral. The participants indicated when they recognized that the same individual's face was repeated, regardless of expression. [5]

The MEG scans provided precise information for the researchers to map out the parts of the brain that encode for appearance-based vs. identity-based information, followed by the application of

sophisticated computational methods to measure the real-time brain processes that convert the appearance of a face into the recognition of an individual.

The researchers believe these findings may be useful to understanding disorders related to breakdowns in the brain's visual perception system, such as prosopagnosia, or face blindness, which is the exact same affliction that the Rockefeller monkey experiments claim to address.

The Carnegie-Mellon research is but one example of exciting and superior non-animal research revealing information about the human brain that cannot be obtained from animals.

A wealth of world-class knowledge can be obtained from directly studying the human brain

A range of non-invasive scanning methods enable scientists to uncover the intricate workings of the human brain. Researchers at the University of Texas at Austin recently used functional magnetic resonance imaging (fMRI) to explore the differences in how the brain learns based on age by scanning human volunteers aged 7 through 30. [6]

fMRI is so safe that it has been used on infants and toddlers. A new study from researchers at the Center for Mind and Brain at the University of California, Davis, used fMRI to learn more about how toddlers memorize words. [7]

Researchers taught a group of two- to three-year-olds new, made-up words and tested their retained memories a week later. Then, after the toddlers were asleep, they underwent fMRI as recordings of the previously learned words were played to them.

The scans showed activation of the hippocampus and anterior medial temporal lobe when hearing the new words, and the degree of activation correlated with how well they remembered these words when tested. These sophisticated and complex findings on how the human brain processes language are impossible using monkeys or other animals.

In another study, scientists at Technische Universität Dresden conducted innovative human brain research that led to the discovery of new regions of the brain. [8] By analyzing advanced human neuroimaging data and post-mortem tissue, the researchers revealed two new areas of the visual sensory thalamus. This pioneering work demonstrates the amazing capability to acquire new knowledge when we explore the human brain.

In other research, neuroscientists at Physikalisch-Technische Bundesanstalt in Germany recently worked with magnetoencephalography (MEG) to delve into the brain. MEG works by detecting brain currents from outside the skull, and while it has worked well for studying slow currents, it is less reliable for fast brain currents that last for a mere millisecond. The interdisciplinary team there worked to refine MEG technology by significantly reducing the noise generated by the MEG device and succeeded in detecting brain oscillations produced by a single sensory stimulus. [9]

That study, carried out on healthy volunteers, applied electrical stimulation to a specific nerve at the wrist while correlating it with the part of the brain that was processing the stimuli by using the optimized MEG technology. For the first time, this allowed scientists to observe nerve cells

in the brain responding to a single stimulus. The implications of this highly sensitive MEG can be applied to studying neurological disorders like epilepsy and Parkinson's which are linked to disruptions in the brain's fast signaling.

Non-imaging cerebrovascular studies in humans

Methods other than imaging are also readily available for studying the human brain. Two recent studies used donated human brain samples to create molecular maps of blood vessels in the human brain to reveal their links to dementia. [10] [11]

In one study, researchers at Massachusetts Institute of Technology analyzed cells from post-mortem brain samples and samples donated from brain surgeries. In another study led by scientists from Stanford University and the University of California, San Francisco, a technique called VINE-Seq was used to isolate and analyze blood vessel cells extracted from post-autopsy brain samples from both healthy controls and people diagnosed with Alzheimer's.

In both cases, scientists found several different cell types and differences in the levels of RNA coming from genes associated with a healthy blood-brain barrier. These results shed light on the role of brain blood vessels on dementia and ways to treat brain disorders causing dementia, an area in which animal models have turned up little relevant information for this devastating human disorder.

Surgical brain samples from human patients provide insights impossible using animals

Another modality available for researching the human brain is to study patients undergoing brain surgery for medical reasons, such as to remove a tumor or locate a seizure focus and who volunteer to take part in studies. Many of these patients who are being treated for epilepsy will already have electrodes placed for intracranial recording of brain activity. In this way, a great deal of unique insight can be obtained about the human brain.

A team of researchers at Cedars-Sinai Medical Center in Los Angeles studied human neurons to learn more about "event segmentation", or what marks the beginning and end of a memory as stored in the human brain. [12]

Another study led by NYU Grossman School of Medicine used volunteers undergoing brain surgery to locate the part of the brain involved in controlling the sound of the words used when speaking. [13] Investigators took recordings of the patients' performing standardized reading tests. As they read, their own recordings were played back simultaneously through headphones. Electrical activity was measured in the patients' brains, and from that, scientists located the brain region linked to this activity: the dorsal precentral gyrus. Future studies can explore potential treatments for speed-related disorders. This understanding of the brain's highly refined control of speech was only possible through the use of human-relevant methods rather than animals who do not speak.

Indeed, the use of human-relevant methods of studying the brain enabled neuroscientists to discover a new pathway in the human brain that processes the sounds of language. A 2021 study from University of California, San Francisco opened doors into how the human brain processes

sounds and words, upending results of previous research, much of which was done on monkeys and other animals. [14]

Using a range of human-relevant methods, including electrocortical stimulation, intracranial recordings and surgical ablation, scientists analyzed the cortical processes in human volunteers undergoing brain surgery for medical purposes.

Previously, it was believed that speech processing followed a serial pathway beginning with sound frequencies and then moving on to extracting consonants and vowels, but this study showed that sounds and words are processed simultaneously yet separately from each other. By studying human physiology instead of inapplicable animal models, scientists can reveal the complexities behind human speech and derive much needed treatments.

While it is impossible to detail the full extent of invaluable and ethical human brain research within the scope of this letter, these many substantive examples prove that we don't need monkey experiments to study the human brain.

Human brains deviate significantly from monkey brains

Despite their extensive use in biomedical and behavioral research, monkeys have failed to provide adequate information to inform human neuroscience and corresponding medical treatments.

As a result, there is growing skepticism by scientists about the validity and justification of primate research. Soroush Seifirad, MD, a researcher and physician at Harvard Medical School has written:

> "With no doubt, neuroscience is the most conflicting field of animal modeling. Compared to any other organ, complexity of the human brain is not comparable with animal models not even in primates. Neuropsychological disorders in human are not comparable to animals at all. That is why a large number of drug discoveries in this field were the result of direct human observations." [15]

Evidence continues to mount, showing that this disparity between human and monkey brains is significant and adversely impacts the translation of results from primate brain research.

Research at the Donders Institute for Brain, Cognition and Behaviour in the Netherlands has shown that differences between the brains of humans and monkeys are more significant than previously believed. [16] Using modern imaging techniques to study the brains of humans and monkeys, a 2020 publication from Donders showed that monkey brains deviated greatly from human brains in their size and connectivity.

The concept of connectivity, referring to the interactions and patterns between neural activity throughout the brain, is central to understanding how the brain processes information. Thus, disparities in brain connectivity are not superficial or tangential to brain function.

The Donders study showed that the differences in brain connectivity between chimpanzees, macaques and human brains were larger than previously believed, particularly in the fasciculus arcuatus, the portion of the brain involved in processing language.

In another study, a comparison of single neuron recordings from the brains of both humans and macaque monkeys showed that there are key differences in the signals from the amygdala and cingulate cortex which likely make humans more susceptible to psychiatric diseases. [17]

It should be pointed out that CAARE does not support the use of monkeys for such research as cited in the prior two examples, though we present them for the evidence they provide of the disparities between human and monkey brains. While both these studies conclude that such information will enhance animal experiments, we believe they are undeniable evidence of the shortcomings of such experiments. A full discussion of the differences between human and monkey brains encompasses far more than these two recent studies.

Animal experiments raise serious moral questions

There can be no question that the ethics of using monkeys for experiments (and indeed, all animals) is deeply problematic. Monkeys are used in this line of brain research for their intelligence and similarities to humans, precisely the reasons that subjecting them to a life of confinement, social deprivation, and experimental procedures is controversial.

Monkeys are deeply sensitive and highly intelligent primates who exhibit keen intelligence that enables them to comply with complex tasks, such as interacting through video games. Their social structure is strong and complex. Mother macaques have been observed to remain bonded with a deceased baby for long periods, extending several days, in a clear demonstration of mourning the baby's loss.

When we engage human subjects in research their participation is voluntary, and their lives can continue. Volunteers give informed consent, understand the full extent of their involvement in the research and generally stand to benefit from it. When the experiment is over, they go home to loved ones who are supportive of their illness or physical challenges. They are able to communicate any distress readily and receive treatment for it. They can opt out of the study.

No such benefits exist for monkeys in a research study. There is no "going home" for them, indeed they have no home. There is no comfort from friends, family, or peers. Being involved in research involves lifetime confinement, isolation, and deprivation of all that is normal to them, including moving freely in a natural environment. They endure prolonged restraint in full body confining devices, fluid deprivation to be motivated to comply with research protocols, and multiple brain surgeries. It is impossible to describe the full extent of their suffering from a life in cages as a forced research subject.

This disturbing situation is compounded by the fact that we now have modern methods that enable us to carry out human relevant research that is not only more humane but delivers superior results for medical progress. It is becoming increasingly harder to justify the use of animals as stand-ins for human research.

As stated in the International Guiding Principles for Biomedical Research Involving Animals, [18] "The use of animals for scientific and/or educational purposes is a privilege that carries with it moral obligations and responsibilities for institutions and individuals to ensure the welfare of these animals to the greatest extent possible. … **Animals should be used only when necessary and only when their use is scientifically and ethically justified."** [emphasis added].

We do not believe that Rockefeller University can meet this requirement and that the experiments on monkeys in the Laboratory of Neural Systems should be terminated. This includes the experiments on marmosets in the same lab, though we have not discussed those in this letter. The same guiding principles apply to those experiments, of inapplicability and ability to be replaced by more relevant human research.

The evolving role of science

We know that while science, by definition, is rooted in natural principles, it is in fact subjective and has changed throughout history. Knowledge evolves, and with it, the underpinnings of what we call science. Examples abound from the belief that leeches hold medical benefit to the earth's relationship to the sun. A more recent example includes our understanding of the biology behind gender identity and baseless aversive therapies. We can point to centuries of beliefs that genetic differences affirmed the "superiority" of the Caucasian race, allowing African Americans to be used in slavery and later experiments.

After the abject failure of chimpanzees in HIV/AIDS research and other areas, they are no longer used for any research in the U.S. (or elsewhere), a decision issued by the U.S. Institute of Medicine in 2011. [19] As stated by David Johnson, vice president of Cascade Biosciences, Inc., "The chimpanzee is no longer an essential model in biomedical research." [20] His statement reflects a radical shift from when chimpanzees were bred aggressively by the federal government in the 1980s for use in HIV/AIDs research. Chimpanzee research was singled out for scrutiny by government largely because of the huge cost and difficulty of maintaining them in labs. Similar criticisms can be made for all areas of animal research.

Not only is science influenced by changes in thought and society, it is also influenced by money. As recently as 2014, otolaryngologists paid by the tobacco industry served as expert witnesses to assert that heavy smoking did not cause throat and neck cancer, but that cleaning solvents, salted fish and mouthwash were the culprits.

Dr. Robert Jackler, professor and chair of otolaryngology at Stanford University conducted extensive research into the testimony by physicians for the tobacco industry between 2009 to 2014, concluding "they used scientifically invalid methods to support their testimony." [21]

Money's ability to influence scientific thought is a woeful reality that must be resisted. The millions of dollars that Rockefeller receives each year from the Freiwald experiments should not cause the administrators and trustees to turn a blind eye to their shortcomings. Do not forget that federal grants are available to carry out excellent human clinical research and that this should be your focus.

Science is not simply generating data, but it has an ethical obligation to address our unmet needs. As Rockefeller states on its website, the university is "in pursuit of one mission: to conduct science for the benefit of humanity."

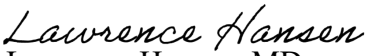
Rockefeller can only pursue this mission by carrying out leading-edge, superior, human-centered research, not outdated and inhumane monkey experiments. The university is well-positioned to undertake such research, with an affiliated hospital and surrounded by other prominent medical centers.

We urge Rockefeller University in the strongest possible terms to abandon these ruthless and scientifically inferior experiments on animals and instead to study the workings of the human brain in the most efficient, ethical and advanced manner possible.

We appreciate your attention to this letter and hope and trust that you will give it your utmost consideration.

Sincerely,

Barbara Stagno, RN. President
Citizens for Alternatives to Animal Research and Experimentation



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