February 10, 2021

Nathan O. Hatch President Wake Forest University 1834 Wake Forest Road Winston-Salem, NC 27109

Via e-mail: nhatch@wfu.edu

Dear President Hatch:

I am writing on behalf of People for the Ethical Treatment of Animals (PETA) and our more than 6.5 million members and supporters to share concerns with you regarding the involvement of one of your faculty members in experiments that inflicted extreme harm to vulnerable monkeys at Chongqing Medical University in China. As detailed below, Carol A. Shively of the Department of Pathology at Wake Forest School of Medicine co-authored a paper (attached here for your reference), published last month, that reports experiments in which sensitive and intelligent monkeys were subjected to unrelenting and extreme torments so egregious that we do not believe such experiments would be approved in the U.S. Not only does this appear to be a case of ethics dumping wherein cruel experiments on animals were conducted in a country that has comparatively weaker ethical and legal protections for them, but as reported in the paper, U.S. taxpayer dollars entrusted to Wake Forest University and Institutional Official Christopher O'Byrne via a National Institutes of Health (NIH) grant were used to fund these experiments at an institution that does not have the necessary approvals required by the NIH.

Inducing Depression in Monkeys

In the 2021 paper co-authored by Shively, adolescent cynomolgus macaques were caged alone—without access to members of their own species—for 80 days. Each day for 55 of those days, they were subjected to two stressors delivered in an unpredictable pattern (please see the figure below, taken from the paper itself). The monkeys were blasted with a loud, 100 dB buzzing noise for 12 hours. They were kept thirsty, deprived of water or any other fluids for 12 hours. They were kept hungry, deprived of food for 24 hours. The monkeys were placed in a cage barely bigger than their bodies and in which their movement was severely restricted for four hours. They were sprayed with cold, 10 degree C water for 10 minutes. They were exposed to a flashing stroboscope for 12 hours. And they were subjected to inescapable and repeated electric shocks on their feet for up to 90 seconds. In short, these monkeys were tortured.

The stated purpose of these chronic, unpredictable torments was to induce depression in the adolescent monkeys. The monkeys exhibited signs of depression, assuming a "huddle posture," clasping themselves with their heads at or below the shoulders while awake; spending less time moving; and also showing a disinterest in items such as apples that would normally bring pleasure.



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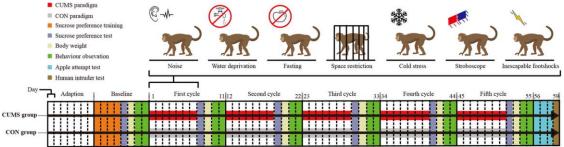
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The authors also subjected the monkeys to the human-intruder test, which they write "is widely used as a challenge test to elicit anxiety-like behaviors" in monkeys.

Most disturbing, the experimental protocol described in the paper is proposed by the authors as a "paradigm" to create "a promising model" to study depression. In other words, other experimenters are being encouraged to follow the trajectory mapped out by Shively and her coauthors, repeating the torture outlined in the paper as a *starting point* from which to then carry out additional experiments on the broken animals.



Teng, T., Shively, C.A., Li, X. *et al.* Chronic unpredictable mild stress produces depressive-like behavior, hypercortisolemia, and metabolic dysfunction in adolescent cynomolgus monkeys. *Translational Psychiatry* **11**, 9 (2021).

Irrelevant to human health

While there is no circumstance in which the torture of monkeys described in the paper authored by Shively and her colleagues could be considered acceptable, the conduct is particularly reprehensible when we consider that several critical limitations inherent in the experiments severely limit their applicability to human depression.

The types of stressors inflicted on primates by Shively and her colleagues do not adequately represent the social and physical stressors that precipitate mental illness in humans. In reality, sexual abuse, physical abuse, substance use disorders, difficulties in interpersonal relationships, economic stress, and chronic illness or injury are more common life traumas associated with mental illnesses and often co-occur in affected individuals. Further, even the monkeys used as a "control group" in the reported experiments spend much of their time in barren, metal cages, and are subject to constant experimental testing. These living conditions cannot provide an accurate example of "typical" or "healthy" development for any species, and the additional stress of laboratory conditions confounds the experimental stressors introduced in this study. Additionally, fundamental differences in gene expression, brain anatomy and physiology, and development among humans and other primates further limit the likelihood these experiments will have any bearing on our understanding or treatment of human depression.

Misuse of American Tax Dollars

According to the paper authored by Shively and her colleagues, the experiments described above were carried out at Chongqing Medical University in Chongqing, China. The paper also specifies that the "research was supported by [grants from several Chinese programs] and the National Institutes of Health (R01HL087103 to C.A.S.)."

The <u>Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals</u> (PHS Policy) states explicitly:

No activity involving animals may be conducted or supported by the PHS until the institution conducting the activity has provided a written Assurance acceptable to the PHS, setting forth compliance with this Policy.

Moreover, Section 4.1.1.1 of the <u>NIH Grants Policy Statement</u> to which Shively, as a recipient of an NIH grant, is expected to adhere is also clear:

No costs for activities with live vertebrate animals may be charged to NIH grants in the absence of a valid Assurance on file with OLAW [NIH's Office of Laboratory Animal Welfare].

And Section 4.1.1.4 of the NIH Grants Policy Statement further advises:

When the recipient is a domestic institution and performance sites are foreign (i.e., domestic grant with a foreign component), PHS Policy requirements are applicable. Accordingly, the recipient remains responsible for animal activities conducted at the foreign site and must provide verification of IACUC approval (i.e., certification that the activities as conducted at the foreign performance site are acceptable to the recipient). The recipient IACUC may accept, as its own, the approval of a foreign organization's IACUC; however, the recipient IACUC remains responsible for the review. Additionally, the foreign site must obtain an Animal Welfare Assurance for Foreign Institutions as described [earlier].

However, Chongqing Medical University is absent from NIH's list, "Institutions with a PHS Approved Animal Welfare Assurance" (please see: <u>https://olaw.nih.gov/assured/app/index.html</u>). Thus, Shively's use of her NIH grant money to help fund the Chongqing monkey experiments is a clear violation of both PHS Policy and the NIH Grants Policy Statement.

Failure of Institutional Oversight

It appears that Wake Forest University's Institutional Animal Care and Use Committee (IACUC) did not review the experiments conducted on monkeys at Chongqing Medical University, as this is not mentioned the published paper. As IACUCs are a keystone of animal experimentation oversight in the U.S., intended to serve as animals' last line of defense, this is problematic.

If the IACUC did review and approve the catastrophically flawed and obscenely unethical experiments, this would suggest that the committee is incapable of carrying out an elementary harm-benefit analysis and also suggest disregard for Principle II of the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, that "Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society." It would also implicate the IACUC in the ethics dumping described earlier.

If the IACUC was aware that Shively had used some of her NIH grant to fund the Chongqing experiments but the committee did not review or approve the experiments, this would represent a failure on the part of the oversight body to carry out its legally mandated responsibilities. In the grant held by Shively and used in the Chongqing experiments, Wake Forest University is identified as the "Awardee Institution"; thus, the school's IACUC would have been responsible for ensuring proper stewardship of the funds.

Conclusion

It is abundantly clear that Wake Forest University is responsible for U.S. tax dollars being used to fund cruel and pointless experiments on monkeys at an institution in China not authorized to use funds from the National Institutes of Health to carry out any experiments on animals.

We urge you to order an investigation into this matter. Should you find that Shively ran afoul of the terms and conditions of her NIH grant as they apply to the use of animals in experiments and that Wake Forest's IACUC also failed in its obligations, we ask that you take appropriate disciplinary action, including disbarring Shively from any future use of animals in experiments and dissolving the IACUC.

Thank you for your time and consideration.

Sincerely,

Kith Re

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