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Julio Licinio, MD, PhD, MBA, MS
Editor-in-Chief
Translational Psychiatry
Via email: licinioj@upstate.edu

Dear Dr. Licinio:

I am writing today as a neuroscientist and on behalf of People for the Ethical Treatment of Animals and our more than 6.5 million members and supporters worldwide to ask that you retract the recently published paper in *Translational Psychiatry*, "Chronic unpredictable mild stress produces depressive-like behavior, hypercortisolemia, and metabolic dysfunction in adolescent cynomolgus monkeys" (https://doi.org/10.1038/s41398-020-01132-6). The experiments described in this paper involve inflicting extreme harm to intelligent vulnerable monkeys, were conducted under specious scientific reasoning, and have little if any relevance to human health.

In their paper, Teng, *et al*. describe how they housed adolescent cynomolgus macaque monkeys alone—without access to members of their own species—for 80 days. Each day for 55 of those days, they were subjected to two of the following stressors in an unpredictable pattern: loud noise for 12 hours, water or food deprivation, space restriction, cold stress, exposure to a stroboscope for 12 h and inescapable shocks to their feet (see figure on the following page). Essentially, monkeys were tortured for these experiments. The proposed goal of these procedures was to create an adolescent monkey "model of depression." However, several critical limitations inherent in these extraordinarily cruel experiments severely limit their applicability to human depression.

The type of stressors inflicted on primates by Teng, *et al*. do not adequately represent the type of 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 affiliated with mental illnesses and often co-occur in affected individuals.[1,2] Any applicability of a nonhuman primate model to human depression is unlikely, especially considering the existence of dramatically different human cultures with different social structures.

Further, even the monkeys used as a control group in most of these 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 confound the experimental stressors introduced in this study. Additionally, fundamental differences in gene expression,[3,4,5,6] brain anatomy and physiology,[7,8,9,10] and development[11,12] among humans and other primates further limit the likelihood these experiments will have any bearing on human depression.

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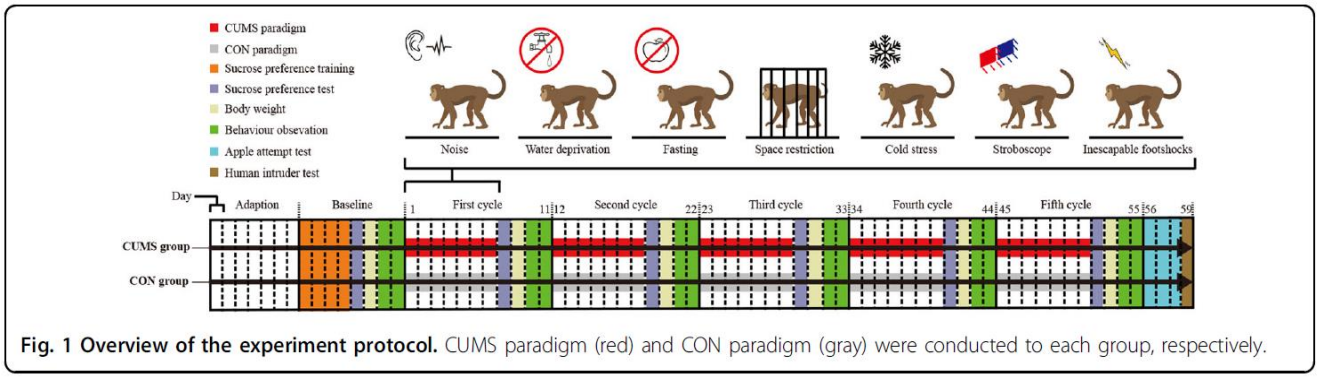

Fig. 1 Overview of the experiment protocol. CUMS paradigm (red) and CON paradigm (gray) were conducted to each group, respectively.

These extremely harmful studies cannot properly model the complex relationship of mental illness and therapeutic response in the human population.

We are aware that Teng, *et al*. assured the journal that they followed guidelines based on "ethics," as stated in the Methods section:

> "Animals were maintained under an experiment protocol approved by the Ethics Committee of Chongqing Medical University (approval no.: 20180705) in accordance with the recommendations of 'The use of non-human primates in research'13 and 'Guide for the Care and Use of Laboratory Animals'14. We also performed matched pairs design to minimize the number of subjects, while maintaining statistical power following the principle of NC3Rs (National Centre for the Replacement, Reduction and Refinement, https://www.nc3rs.org.uk/)."

However, these assurances were quite obviously not enough to prevent the described experiments from occurring, despite their significant ethical and scientific shortcomings. A reputable journal cannot rely on these statements alone to decide what is acceptable to publish—editors also have an important role in holding the research they accept for publishing to a rigorous, humane standard. In the case of these experiments, the incredible suffering the authors claimed to "minimize" was the entire point of these experiments.

The scientific publishing community must take a strong position to publish only rigorous and ethical research. **Will *Translational Psychiatry* retract this paper and conduct an investigation to determine how such a paper passed your peer review process?**

Sincerely,

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