January 22, 2024

John J. Ngai, Ph.D. Director Brain Research Through Advancing Innovative Neurotechnologies Initiative National Institutes of Health

Via e-mail: john.ngai@nih.gov

Dear Dr. Ngai:

I'm writing as a neuroscientist and on behalf of People for the Ethical Treatment of Animals (PETA) regarding a series of visual deprivation experiments funded by the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative being performed on infant rhesus macaques in a laboratory at Harvard Medical School (HMS). The experiments, supported by Project <u>R01NS123778</u> and titled "Effects of abnormal early experience on IT circuitry," are currently receiving \$2,039,107 in funding from the BRAIN Initiative. As will be reviewed below, these experiments involve performing exceptionally harmful procedures on infant rhesus macaques that are not only unethical, but outdated and redundant. It is, quite frankly, shocking that these experiments are part of the BRAIN Initiative's efforts towards "revolutionizing our understanding of the human brain" with "a common goal of accelerating the development of neurotechnologies."

Irreversible Harms

The experiments in question, led by Principal Investigator Margaret Livingstone, subject newborn rhesus macaques to both maternal and sensory deprivation. More specifically, they involve permanently removing infant monkeys from their mothers at birth and subjecting them to various sensory visual deprivation procedures. These visual deprivation procedures, shockingly, include forcing these newborn infants to wear helmets and goggles that create stroboscopic effects for the first 18 months of their life. Other visual deprivation procedures in this project include raising these maternally-deprived infants with goggles that invert their visual input or alternatively occlude their right and left eyes for at least their first year of life. After being removed from their mothers and having their visual input disrupted, impeded, or warped these monkeys then have their entire skulls encased in an acrylic shell so that the experimenters can attach a head fixation device and implant electrodes into their brains.

It's well established that mother-deprived infant monkeys like the ones in this laboratory experience both immediate and long-term effects from this deprivation. Monkeys separated from their mothers exhibit excessive fearfulness and/or aggression,¹ produce excess stress hormones,² display abnormal

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reproductive behavior, and frequently rank at the bottom of the social-dominance hierarchy.³ Maternally deprived macaques are more likely to engage in self-injurious behavior,⁴ exhibit motor stereotypies indicative of frustration and stress,⁵ experience abnormal sleep patterns,⁶ and demonstrate increased startle and stress responses to threatening stimuli,⁷ and they are more susceptible to infection.⁸

Additionally, maternal deprivation affects brain structure and function. Monkeys "hand-reared" in a laboratory setting exhibit altered serotonin pathway function^{9,10} and cerebral blood flow¹¹ as well as altered levels of brain-derived neurotrophic factor and nerve growth factor critical for normal brain function.¹² Maternal deprivation also has long-term effects on brain morphology,¹³ including in the cortical regions that Livingstone is studying.¹⁴ These substantive brain alterations not only reflect the atypical development these animals are being forced to experience but also influence the generalizability of Livingstone's own neurological data. As the purported purpose of these experiments is to selectively study the impact of visual deprivation on these animals' cortical and visual processing development, ignoring the various neurological effects of the additional maternal deprivation is problematic and potentially misleading.

These already emotionally and physically damaged monkeys are then forced to live in what can only be described as a visually confusing and terrifying world, with their vision continuously and ultimately permanently disrupted. Moreover, these sorts of visual deprivation procedures are known to cause permanent retinal damage (including retinal detachment in some species), balance and gait abnormalities, in addition to the expected visual deficits and visual system aberrations the experimenters are trying to induce. In fact, brief stroboscopic conditions are frequently used as both chronic and acute stressors in animals in laboratories due to their long-and short-term effects on the animals' physical and psychological well-being.^{15,16,17,18} The impact of 18 months of strobe lighting on the overall health of these monkeys is likely to be profound, but was not taken into consideration when evaluating the harms induced by these experiments against their purported scientific merits.

Unnecessary Harms

The purported purpose of these experiments is to "explore how specific abnormal early visual experience changes neuronal selectivity." However, these sorts of visual deprivation experiments have been performed *ad nauseum* for the past 50 years in a host of animal species, including goldfish,¹⁹ chickens,²⁰ rats,^{21,22} songbirds,²³ frogs,²⁴ rabbits,^{25,26,27} guinea pigs,²⁸ cats,^{29,30,31,32,33} *and* nonhuman primates.^{34,35,36,37} The only novelty Livingstone is bringing with this 2-million-dollar project is the extreme length of time she (and the BRAIN initiative) are willing to subject these monkeys to strobe-, prism-, and binocular deprivation-rearing. The fact that to date no one has decided to force infant macaques to live under stroboscopic lighting conditions for the first 18 months of their life doesn't make these experiments scientifically innovative, just ethically unprecedented.

There are a multitude of projects using noninvasive methods with humans to study the impact of early sensory experience on neural and visual development. For example, research with humans who experience early transient congenital blindness,^{38,39,40,41} amblyopia,⁴² and visual impairments⁴³ have investigated the effects of abnormal early visual experience on the development of vision and other senses, eye-tracking behavior, neural reorganization, and domain-specific visual abilities. Researchers have also studied the effect of short-term monocular deprivation in human volunteers and its effects on binocular rivalry,⁴⁴ visual evoked potentials,⁴⁵ and BOLD activity in the visual cortex.⁴⁶ and have assessed the neurochemical mechanisms associated with plasticity in the visual cortex.⁴⁷ In addition to being human-relevant, these studies don't have the numerous confounds of maternal deprivation introduced by the experiments performed in Livingstone's laboratory.

Conclusion

Given the cruelty inherent in the procedures performed under Project R01NS123778, their complete redundancy to the field, and the availability of modern, non-invasive methods, it's concerning that the BRAIN Initiative, which prides itself on the advancement of innovative technologies to revolutionize our understanding of the *human* brain, has invested in these experiments.

Hundreds of scientists have already openly objected to these experiments on both ethical and scientific grounds. It is horrifying that they are being allowed to continue because the handful of people reviewing this grant found these procedures morally acceptable. They are not. Please discontinue your support for this project. I would be happy to meet with you to discuss this important matter.

Sincerely,

At Re

Chief Scientist Laboratory Investigations Department

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