

#### DEPARTMENT OF HEALTH & HUMAN SERVICES

#### PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare 6700B Rockledge Drive, Suite 2500, MSC 6910 Bethesda, Maryland 20892-6910

Home Page: http://grants.nih.gov/grants/olaw/olaw.htm

October 26, 2022

FOR EXPRESS MAIL:
Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 480-3387

Re: Animal Welfare Assurance A3431-01 [OLAW Case 90]

### MEMORANDUM FOR RECORD

The Office of Laboratory Animal Welfare (OLAW) has determined that the October 12, 2022 letter from (b) (6) of People for the Ethical Treatment of Animals (PETA) regarding the NEI sponsored study (5R01EY025670) at the Harvard Medical School contains no allegations of noncompliance with the PHS Policy and OLAW will therefore not initiate an investigation. This case is thereby administratively closed as of this date.

Signed,

Digitally signed by Brent C. Morse -S

Date: 2022.10.26 16:34:27

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

73431-90

PETA

October 12, 2022

Michael F. Chiang, M.D. Director National Eye Institute National Institutes of Health

Via e-mail: michael.chiang@nih.gov

Dear Dr. Chiang:

Good morning. I'm writing as a neuroscientist and on behalf of People for the Ethical Treatment of Animals (PETA) regarding a series of experiments funded by the National Eye Institute (NEI) being performed on infant rhesus macaques in a Harvard Medical School (HMS) laboratory. The experiments in question, led by Principal Investigator Margaret Livingstone, subject newborn rhesus macaques to both maternal and sensory deprivation.

After reviewing the publications from this laboratory, I'm deeply concerned that the harm caused to the animals far outweighs any potential benefits to human or animal health. I urge NEI to discontinue its support of this project in favor of modern, humane research.

The experiments supported by Project <u>5R01EY025670</u>, titled "Development of Domains in Inferotemporal Cortex," involve removing infant monkeys from their mothers at birth and subjecting them to various sensory deprivation procedures, including binocular deprivation and monocular deprivation. In addition, the faces of individuals seen by the infants are obscured from their vision. In some experiments, newborn monkeys' eyes are sutured closed for their entire first year of life. In other experiments, monkeys are denied the opportunity to view the faces of conspecifics or even the laboratory workers feeding them.\text{! In fact, these laboratory workers were required to wear welding masks during their limited interactions with the infants. Monkeys in this laboratory are subjected to multiple major life surgeries so that head posts can be affixed to their skulls\(^2\) or eye coils\(^3\) and/or multiple intracranial electrode arrays can be implanted.\(^4\) For multiple experiments, their heads are immobilized using helmets, chin straps, and bite bars,\(^5\) and in some experiments the monkeys are killed and dissected.

It's well established that mother-deprived infant monkeys, whether they're raised by surrogates, by lab staff, or in peer groups, experience both immediate and long-term effects from this deprivation. Monkeys separated from their mothers exhibit excessive fearfulness and/or aggression,<sup>6</sup> produce excess stress hormones,<sup>7</sup> display abnormal reproductive behavior, and frequently rank at the bottom of the social-dominance hierarchy.<sup>8</sup> Maternally deprived macaques are more likely to engage in self-injurious behavior,<sup>9</sup> exhibit motor stereotypies indicative of frustration and stress,<sup>10</sup> experience abnormal sleep patterns,<sup>11</sup> and

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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demonstrate increased startle and stress responses to threatening stimuli, 12 and they are more susceptible to infection. 13

Additionally, maternal deprivation affects brain structure and function. Monkeys "hand-reared" in a laboratory setting exhibit altered serotonin pathway function 14,15 and cerebral blood flow 16 as well as altered levels of brain-derived neurotrophic factor and nerve growth factor critical for normal brain function. 17 Maternal deprivation also has long-term effects on brain morphology, 18 including in the cortical regions that Livingstone is studying. 19 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.

The purported purpose of these experiments is to "explore how specific abnormal early visual experience changes neuronal selectivity." However, 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, 20,21,22,23 amblyopia, 24 and visual impairments 25 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, 26 visual evoked potentials, 27 and BOLD activity in the visual cortex 28 and have assessed the neurochemical mechanisms associated with plasticity in the visual cortex. In addition to being more human-relevant, these studies don't have the numerous confounds of maternal deprivation introduced by the experiments performed in Livingstone's laboratory.

It's possible that members of the grant review committee may have been unaware of the express harm that these experiments cause or the available alternatives when scoring the application. Publications from this laboratory don't provide any detailed descriptions of the various surgical procedures performed on the monkeys, nor do they indicate what, if any, type of pre-surgical analgesia, anesthesia, or post-operative pain medication or monitoring are provided. These same publications also omit whether these animals were deprived of food or water to ensure their cooperation on behavior tests with rewards of juice. Also absent is any detailed information about the specific "hand-rearing" procedures that these monkeys experience, including whether a surrogate is provided, what types of enrichment these monkeys may or may not receive, or what socialization with peers they are allowed or disallowed. In fact, papers coming out of this laboratory are so absent of any methodological detail that it's hard not to assume some sort of deliberate obfuscation is taking place. Regardless, the experimenters in this laboratory do not appear interested in sharing the methodological details or the full impact of their experiments with the scientific community.

Given the cruelty inherent in the procedures performed under Project 5R01EY025670 and the availability of non-invasive methods, it's concerning that NEI has invested \$3,775,193 into these experiments. Please discontinue your support of this project. I would be happy to meet with you to discuss this important matter.

Sincerely,



<sup>1</sup>Arcaro MJ, Mautz T, Berezovskii VK, Livingstone MS. Anatomical correlates of face patches in macaque inferotemporal cortex. *Proc Natl Acad Sci U S A*. 2020;117(51):32667-32678.

<sup>2</sup>Ponce CR, Hartmann TS, Livingstone MS. End-stopping predicts curvature tuning along the ventral stream. *J Neurosci*. 2017;37(3):648-659.

<sup>3</sup>Howe PD, Livingstone MS. V1 partially solves the stereo aperture problem. Cereb Cortex. 2006;16(9):1332-1337.

<sup>4</sup>Arcaro MJ, Ponce C, Livingstone M. The neurons that mistook a hat for a face. *Elife*, 2020;9:e53798.

<sup>5</sup>Arcaro MJ, Livingstone MS. Retinotopic organization of scene areas in macaque inferior temporal cortex. *J Neurosci*. 2017;37(31):7373-7389.

<sup>6</sup>Suomi SJ. Early determinants of behaviour: evidence from primate studies. *Br Med Bull*. 1997;53(1):170–184. 
<sup>7</sup>Feng X, Wang L, Yang S, et al. Maternal separation produces lasting changes in cortisol and behavior in rhesus monkeys [published correction appears in *Proc Natl Acad Sci U S A*. 2012 Jul 24;109(30):12260].

<sup>8</sup>Dettmer AM, Novak MA, Suomi SJ, Meyer JS. Physiological and behavioral adaptation to relocation stress in differentially reared rhesus monkeys: hair cortisol as a biomarker for anxiety-related responses. *Psychoneuroendocrinology*, 2012;37(2):191-199.

<sup>9</sup>Drago L, Thierry B. Effects of six-day maternal separation on Tonkean macaque infants. *Primates*. 2000;41(2):137–145.

<sup>10</sup>Barr CS, Becker M L, Suomi SJ., Higley JD. Relationships among CSF monoamine metabolite levels, alcohol sensitivity, and alcohol-related aggression in rhesus macaques. *Aggressive Behavior*. 2005. 29(4), 288-301.

<sup>11</sup>Barrett CE, Noble P, Hanson E, Pine DS, Winslow JT, Nelson EE. Early adverse rearing experiences alter sleep-wake patterns and plasma cortisol levels in juvenile rhesus monkeys. *Psychoneuroendocrinology*. 2009;34(7):1029-1040.

<sup>12</sup>Nelson EE, Herman KN, Barrett CE, et al. Adverse rearing experiences enhance responding to both aversive and rewarding stimuli in juvenile rhesus monkeys. *Biol Psychiatry*. 2009;66(7):702-704.

<sup>13</sup>Bailey MT, Coe CL. Maternal separation disrupts the integrity of the intestinal microflora in infant rhesus monkeys. *Dev Psychobiol*. 1999;35(2):146-155.

<sup>14</sup>Bennett AJ, Lesch KP, Heils A, et al. Early experience and serotonin transporter gene variation interact to influence primate CNS function. *Mol Psychiatry*. 2002;7(1):118-122.

<sup>15</sup>Spinelli S, Chefer S, Carson RE, et al. Effects of early-life stress on serotonin(1A) receptors in juvenile rhesus monkeys measured by positron emission tomography. *Biol Psychiatry*, 2010;67(12):1146-1153.

<sup>16</sup>Ichise M, Vines DC, Gura T, et al. Effects of early life stress on [11C]DASB positron emission tomography imaging of serotonin transporters in adolescent peer- and mother-reared rhesus monkeys. *J Neurosci*. 2006;26(17):4638-4643.

<sup>17</sup>Cirulli F, Francia N, Branchi I, et al. Changes in plasma levels of BDNF and NGF reveal a gender-selective vulnerability to early adversity in rhesus macaques. *Psychoneuroendocrinology*. 2009;34(2):172-180.

<sup>18</sup>Spinelli S, Chefer S, Suomi SJ, Higley JD, Barr CS, Stein E. Early-life stress induces long-term morphologic changes in primate brain. *Arch Gen Psychiatry*. 2009;66(6):658-665.

<sup>19</sup>Wang J, Feng X, Wu J, et al. Alterations of gray matter volume and white matter integrity in maternal deprivation monkeys. *Neuroscience*. 2018;384:14-20.

<sup>20</sup>Guerreiro MJ, Putzar L, Röder B. The effect of early visual deprivation on the neural bases of multisensory processing. *Brain*. 2015;138(Pt 6):1499-1504.

<sup>21</sup>Bottari D, Kekunnaya R, Hense M, Troje NF, Sourav S, Röder B. Motion processing after sight restoration: no competition between visual recovery and auditory compensation. *Neuroimage*. 2018;167:284-296.

<sup>&</sup>lt;sup>22</sup>Ossandón JP, Zerr P, Shareef I, Kekunnaya R, Röder B. Active vision in sight recovery individuals with a history of long-lasting congenital blindness [published online ahead of print, 2022 Sep 26]. *eNeuro*. 2022;ENEURO.0051-22.2022.

<sup>&</sup>lt;sup>23</sup>Guerreiro MJS, Kekunnaya R, Röder B. Top-down modulation of visual cortical processing after transient congenital blindness. *Neuropsychologia*. 2022;174:108338.

<sup>&</sup>lt;sup>24</sup>Ghasia F, Wang J. Amblyopia and fixation eye movements. *J Neurol Sci.* 2022;441:120373. doi:10.1016/j.jns.2022.120373

<sup>&</sup>lt;sup>25</sup>Collignon O, Voss P, Lassonde M, Lepore F. Cross-modal plasticity for the spatial processing of sounds in visually deprived subjects. *Exp Brain Res*, 2009;192(3):343-358.

<sup>&</sup>lt;sup>26</sup>Lunghi C, Burr DC, Morrone C. Brief periods of monocular deprivation disrupt ocular balance in human adult visual cortex. *Curr Biol.* 2011;21(14):R538-R539.

<sup>&</sup>lt;sup>27</sup>Lunghi C, Berchicci M, Morrone MC, Di Russo F. Short-term monocular deprivation alters early components of visual evoked potentials. *J Physiol*. 2015;593(19):4361-4372.

<sup>&</sup>lt;sup>28</sup>Binda P, Kurzawski JW, Lunghi C, Biagi L, Tosetti M, Morrone MC. Response to short-term deprivation of the human adult visual cortex measured with 7T BOLD. *Elife*. 2018;7:e40014.

<sup>&</sup>lt;sup>29</sup>Sheynin Y, Chamoun M, Baldwin AS, Rosa-Neto P, Hess RF, Vaucher E. Cholinergic potentiation alters perceptual eye dominance plasticity induced by a few hours of monocular patching in adults. *Front Neurosci*. 2019;13:22.

<sup>&</sup>lt;sup>30</sup>Arcaro MJ, Schade PF, Vincent JL, Ponce CR, Livingstone MS. Seeing faces is necessary for face-domain formation. *Nat Neurosci*. 2017;20(10):1404-1412.

<sup>&</sup>lt;sup>31</sup>Arcaro MJ, Ponce C, Livingstone M. The neurons that mistook a hat for a face. *Elife*. 2020;9:e53798.

<sup>&</sup>lt;sup>32</sup>Bardon A, Xiao W, Ponce CR, Livingstone MS, Kreiman G. Face neurons encode nonsemantic features. *Proc Natl Acad Sci U S A*. 2022;119(16):e2118705119.

<sup>&</sup>lt;sup>33</sup>Arcaro MJ, Mautz T, Berezovskii VK, Livingstone MS. Anatomical correlates of face patches in macaque inferotemporal cortex. *Proc Natl Acad Sci U S A*. 2020;117(51):32667-32678.



National Institutes of Health Bethesda, Maryland 20892

October 12, 2022



Re: Your letter of October 12

Dear (b) (6)

I am in receipt of your letter of October 12, 2022, which you addressed to Dr. Michael Chiang, Director of the National Eye Institute (NEI).

NIH takes seriously the welfare of laboratory animals. If you have particular concerns about the welfare of laboratory animals, please contact the Director of the Office of Laboratory Animal Welfare at 6700B Rockledge Drive, Suite 2500, MSC 6910, Bethesda, MD 20892 (20817 zip code for delivery service or hand delivery) or by email at olaw@od.nih.gov.

Sincerely yours,

Michael S. Lauer -S Digitally signed by Michael S. Lauer -S Date: 2022.10.12 12:44:44 -04'00'

Michael S Lauer, MD NIH Deputy Director for Extramural Research Director, NIH Office of Extramural Research

# McCoy, Devora (NIH/OD) [E]

From:

Morse, Brent (NIH/OD) [E]

Sent:

Friday, October 21, 2022 2:08 PM

To:

McCoy, Devora (NIH/OD) [E]

Subject:

FW: Letter from PETA

Attachments:

2022-10-12-Letter to NEI[2].pdf; PETA response 10 12 22[1].pdf

Follow Up Flag:

Follow up

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Flagged

Hello Devora,

Please open a case file (A3431) and assign it to me. Thank you.

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Lauer, Michael (NIH/OD) [E] <michael.lauer@nih.gov>

Sent: Wednesday, October 12, 2022 3:51 PM

To: Brown, Patricia [OLAW] (NIH/OD) [E] <br/>
srownp@od.nih.gov>

Cc: Bundesen, Liza (NIH/OD) [E] < Ibundese@mail.nih.gov>; Morse, Brent (NIH/OD) [E] < morseb@mail.nih.gov>; Lauer,

Michael (NIH/OD) [E] <michael.lauer@nih.gov>

Subject: Re: Letter from PETA

Excellent, Pat and Brent, thanks so much!

Mike

From: "Brown, Patricia [OLAW] (NIH/OD) [E]" <br/>
brownp@od.nih.gov>

Date: Wednesday, October 12, 2022 at 3:49 PM

To: "Lauer, Michael (NIH/OD) [E]" <michael.lauer@nih.gov>

Cc: "Bundesen, Liza (NIH/OD) [E]" < lbundese@mail.nih.gov>, "Morse, Brent (NIH/OD) [E]"

<morseb@mail.nih.gov>

Subject: RE: Letter from PETA

Good afternoon Mike,

I have reviewed the letter from PETA and referred it to the Division of Compliance Oversight for their review of the allegations and to take further steps as necessary.

Sincerely,

Pat

Patricia Brown, VMD, MS, DACLAM (she/her)
Director, Office of Laboratory Animal Welfare,
Office of Extramural Research, Office of the Director, NIH

## 301-451-4209, brownp@mail.nih.gov

From: Lauer, Michael (NIH/OD) [E] <michael.lauer@nih.gov>

Sent: Wednesday, October 12, 2022 12:50 PM

To: Brown, Patricia [OLAW] (NIH/OD) [E] <br/>
sprownp@od.nih.gov>

Cc: Lauer, Michael (NIH/OD) [E] <michael.lauer@nih.gov>; Bundesen, Liza (NIH/OD) [E] <lbundese@mail.nih.gov>

Subject: FW: Letter from PETA

Hi Pat - bringing this to your attention.

Many thanks, Mike

From: "Lauer, Michael (NIH/OD) [E]" < michael.lauer@nih.gov>

Date: Wednesday, October 12, 2022 at 12:48 PM

To:

Cc: "Lauer, Michael (NIH/OD) [E]" <michael.lauer@nih.gov>

Subject: Re: Letter from PETA

Dear (b) (6)

Please see attached.

Sincerely, Michael S Lauer, MD

Michael S Lauer, MD
NIH Deputy Director for Extramural Research
Director, NIH Office of Extramural Research
1 Center Drive, Room 144, Bethesda MD 20892
Michael.Lauer@nih.gov

From:

(b) (6)

**Date:** Wednesday, October 12, 2022 at 10:41 AM **To:** Michael Chiang < michael.chiang@nih.gov >

Subject: [EXTERNAL] Letter from PETA

Dear Dr. Chiang:

Good morning. I'm writing as a neuroscientist and on behalf of People for the Ethical Treatment of Animals (PETA) regarding a series of experiments funded by the National Eye Institute (NEI) being performed on infant rhesus macaques in a Harvard Medical School (HMS) laboratory. Please see the attached letter for more details.

Thank you.

(b) (6



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