

ETHICAL AND SCIENTIFIC CONCERNS REGARDING THE CONTINUED USE OF **EXPERIMENTALLY INDUCED BRAIN INJURIES IN PRIMATES**

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INTRODUCTION

For more than a century, researchers have been deliberately inducing permanent, debilitating, and sometimes fatal brain injuries in non-human primates for the purported purpose of gaining insight into the neural bases of human behaviours. These experiments cause irreversible damage in primates, but their contribution to our accurate understanding of human brain-behaviour relationships is questionable, at best. Confounds introduced by the impoverished and stressful conditions inherent to laboratory life, critical species differences, and anatomical imprecision of artificially-induced lesions collectively limit the translational value of these experiments. Here we present data on the current prevalence of these experiments, and discuss the numerous ethical and scientific arguments for the discontinuation of these methods in contemporary neuroscience research.

METHODS

To assess current prevalence of induced lesions in nonhuman primates, we employed a search using PubMed to identify empirical studies since 2010 that created excitotoxic or aspiration lesions in nonhuman primates to study neural correlates of behavior. A comparable search was conducted using <u>NIHReporter</u> to determine funding frequency since 2010. To assess the translational value of these types of experiments, we used NIH's Office of Portfolio Analysis (OPA) tool iCite. Using individual publications citation network, and the Medical Subject Headings (MeSH) of papers within that citation network, the Approximate Potential to Translate (APT) score is a machine learning based estimate of an individual paper's potential to be cited by clinical researchers in the future. The 115 publications identified above were entered into this tool. To assess anatomical precision of lesions created in these types of experiments, available data from the 115 publications were analyzed. Only 89 of 115 publications included lesion extent data, and only 85 included data about unintended brain damage.

ETHICAL CONCERNS

Multiple major-survival surgeries Multiple craniotomies Permanent cranial implants Repeated anesthesia Inadequate pain relief Infection

Permanent brain damage: Impaired reward processing Impaired social skills Impaired learning Impaired visual spatial skills Impaired memory Altered emotional responsivity

Laboratory/Captivity:

Minimal mental stimulation Social Isolation Fear/stress inducing procedures Food and water deprivation Frequent lengthy restraint Chronic and acute stress Self-injurious behaviors Alopecia Lack of autonomy Minimal species specific behaviors



NIH-funded Grants Per Publications Per Year Year 2010-2021 30 2010-2021 20 25 15 20 15 10 10 5 5 0 2010 2011 2012 2013 2013 2014 2015 2015 2017 2017 2019 2019 2019 2019 2010 2011 2012 2013 2014 2015 2015 2016 2019 2019 2019 2020 2020

SCIENTIFIC LIMITATIONS

Laboratory-Induced Confounds



Chronic and acute stress Abnormal stress hormone levels

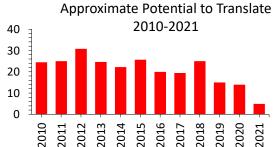
- Altered microbiota
- Cognitive deprivation
- Social deprivation
- Maternal deprivation
- Mismanaged pain
- Self-injurious behaviors
- Altered gene expression

Disruption of normal brain development, organization and function, behaviors

Incomplete Lesion of Region of Interest (ROI)	Lesion Extended Beyond ROI
100%	94%

Limited Clinical Relevance

Anatomical Imprecision



NIH's iCite tool indicates that experiments purposely inducing lesions in monkeys to study the neural correlates of behavior, have, on average, only a 22% chance of ever being cited by a clinical paper.

Human-Relevant Alternatives



CONCLUSIONS

The practice of deliberately inducing permanent brain lesions in non-human primates should be discontinued. The method is imprecise, and the confounds introduced by the procedures involved as well as the laboratory environment, severely limit data from these experiments from having any human-relevant applications.

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References: https://www.peta.org/wp-content/uploads/2021/07/WC-refs-2021.pdf

CURRENT PREVALENCE