# Research Visualization of Future Primate Neuroscience

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## Abstract

Future studies utilizing Non-Human Primates (NHPs) in neuroscience and biomedical fields are still crucial to our efforts to comprehend the intricacies and operation of the mammalian central nervous system. In order to address ongoing and new research problems that can only be addressed in NHP research models, the NHP neuroscience researcher must be permitted to apply cutting-edge technology, such as the use of novel viral vectors, gene therapy, and transgenic techniques. This article's point of view captures these cutting-edge technology and some particular research issues they can resolve. At the same time, we draw attention to some current obstacles to international NHP research and collaborations, such as the absence of universally accepted ethical and regulatory frameworks for NHP research, the restrictions on the export and transportation of animals, and the persistent power of activist groups opposed to NHP research.

**Keywords** Gene therapy • Viral vector approaches • Transgenic • CRISPR/Cas9

## Introduction

Non-Human Primates (NHPs) have been the subject of substantial evaluation in Europe for biomedical research. The Scientific Committee on Health, Environmental and Emerging Risks (SCHEER), which was founded by the European Commission, adopted an opinion on the use of NHPs in 2009 and presented an update to this report in 2017. NHP use was deemed crucial for pharmaceutical advancements, research on infectious disorders, (xeno)transplantation, and neurology in the inaugural SCHEER study. In a similar spirit, the SCHEER committee of 2017 came to the conclusion that a number of significant reasons, at least in the aforementioned domains, contribute to the continuous need for NHPs.

For instance, due to the poor characterization of pharmacokinetic parameters in isolated in vitro systems and the challenges of extrapolating from in vitro data to people, safety testing of drugs and medical devices frequently requires NHPs. Animal models, especially NHPs, cannot accurately represent every aspect of a human illness state, hence there are still significant challenges in extrapolating findings from animal models to humans. However, the committee was remarkably foresighted when it came to infectious diseases, as evidenced by their statement that "new technologies are unlikely to negate the need for infectious NHP models in the near future due to emerging and re-emerging pathogens," which was more than justified in the Covid-19 pandemic. There are still significantlimitations in neuroscience, especially in systems neuroscience. While currently a simple to use technology and non-invasive, functional imaging experiments in human volunteers, for example, actually only yield indirect assessments of neuronal population activity at very low spatio-temporal resolution. The circuitry and functional architecture of the brain, rather than physics or poor engineering, are to blame for the limits of Functional Magnetic Resonance Imaging (fMRI), which are unlikely to be overcome by improving the sophistication and power of the scanners. The fMRI signal is unable to distinguish between bottom-up and top-down signals, function-specific processing from neuromodulation, and it occasionally conflates excitation with inhibition. It is impossible to quantify the strength of the fMRI signal to represent differences between brain areas or between activities within the same region. The latter issue is caused by the fact that hemodynamic responses are sensitive to the size of the activated population, which may change as the sparsity of neural representations varies spatially and temporally, rather than our inability to currently estimate Cerebral Metabolic Rate (CMRO2) accurately from the Blood-Oxygen-Level-Dependent (BOLD) imaging signal. Functional imaging observations, with the exception of those involving structural alterations or localized tissue damage, offer potential interpretations, the selective validation of which frequently necessitates additional invasive research.

### Viral vectors for disease simulation

Although neurotoxin-based mammalian animal models of PD have established the foundation for the majority of our current understanding of basal ganglia function and dysfunction, these models did not successfully reproduce the key neuropathological hallmarks that typically characterize PD (such as dopaminergic cell death triggered by alpha-synuclein (Syn) aggregation). Most crucially, testing neuroprotective, disease-modifying strategies is severely constrained by the acute dopaminergic damage brought on by neurotoxins. The area of animal modeling in PD underwent a significant transformation since it was realized that Syn is the primary component of Lewy bodies. Accordingly, a number of mouse transgenic lines have been made available that overexpress either mutant or wild type versions of Syn, and the majority of these models replicate numerous important characteristics of PD. Although these transgenic mouse lines are interesting testing platforms for novel anti-Syn aggregation treatment possibilities, it is important to keep in mind that neuronal loss in the substantia nigra pars compacta (SNpc) is often weak or nonexistent in most instances. The majority of the transgenic mice that are readily available for Syn aggregation lack the necessary phenotypic. Since synaptic aggregation causes gradual dopaminergic neuronal degeneration, there is currently a definite trend toward the development and characterization of NHP (macaque) models.

### Therapeutic use of viral vectors

In IQVIA's experience, a hybrid strategy would be preferable than a purely virtual one for the majority of oncology clinical studies. For non-interventional research like long-term follow-up studies, the latter is more suitable. Even though most clinical trials could benefit from novel strategies, it's crucial to evaluate each study in light of its own unique characteristics, including its phase (e.g., early versus late phase), the drug or intervention being tested, its mode of action, the route of administration (e.g., oral versus intravenous), its safety and tolerability profile, the patient population, and its objectives and endpoints.

## Conclusion

Governments, funders, policymakers, and the general public must continue to support biomedical researchers who use NHP models if we are to have better healthcare and effective treatments in the near future and beyond. Only then will all of us be able to take advantage of the knowledge generated by these priceless NHP research models.

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