Minireview Article

The Use of Primates as Experimental Models in Scientific Research and Its Ethical Implications

ABSTRACT

Non-human primates (NHPs) are considered ideal experimental models for replicating human diseases, due to their physiological, anatomical and neurological similarities to humans. However, the use of NHPs in research has ethical considerations and requires significant financial and temporal investments, due to the costs involved in the process and evaluation time.In addition to ethical issues and legal protection, research with experimental primate models involves advantages, such as the extreme physiological similarity, and disadvantages, such as the difficulty in establishing parameters for pain management and assessment. This literature review analyzed articles from the Pubmed, Scopus and Web of Science databases published in the last five years. This review included 12 articles that addressed topics such as scientific research, primate therapies, animal welfare and legal protection, highlighting the relevance of NHPs in scientific studies and interest in using these models to understand human diseases in order to develop new therapies. Despite the ethical challenges involved in this issue, it was discussed that it is important to take into account the scientific benefits and ethical considerations, as well as developing alternative methods to reduce the use of primates in research.

Keywords: Animal health; Legal protection; Animal welfare; Non-human primates.

1. INTRODUCTION

Non-human primates (NHPs) are widely regarded as the most suitable animal models for replicating human disease and are often considered the gold standard in drug development and regulatory approval [1]. Due to the advanced nature of experimental technology, establishing NHP animal models requires substantial investments in financial and labor resources. Moreover, their use is limited by ethical considerations, and only a few studies have employed NHP animal models [2].

However, compared to other model organisms, NHPs can more accurately and comprehensively simulate symptoms of human Parkinson's disease (PD), thus providing superior pathways for investigating clinical treatment modalities [3]. Compared to rodents and other organisms, NHPs exhibit a greater similarity to humans in brain structure [4,19,20].

Additionally, the type and distribution of brain cells in NHPs are more complex than in other model organisms, and the normal physiological activities and functional patterns of the brain are more akin to those of humans [5]. As a close evolutionary relative of humans, NHPs

remain highly similar to humans in terms of genetic, physiological, and behavioral diversity [2,17,18]. In light of this, the present study aims to conduct a literature review on experimental models in primates, exploring the advantages, disadvantages, ethical considerations, and legal protections involved in such research.

2. METHODOLOGY

In this literature review, relevant scientific articles were analyzed, extracted from databases such as PubMed, Scopus, and Web of Science, using search terms such as "experimental model in primates," "primates in scientific research," "diseases in primate experimental models," and "laboratory primate welfare''. From the articles found in the PubMed, Scopus, and Web of Science databases using the search terms, PubMed yielded 402,111 results using the term "experimental model in primates," 669,342 results using the term "primates in scientific research," 283,019 results using the term "diseases in primate experimental models," and 1,493 results using the term "laboratory primate welfare." In the Scopus database, 1,026 documents were found using the term "experimental model in primates," 239 documents using the term "primates in scientific research," 532 documents using the term "diseases in primate experimental models," and 5 documents using the term "laboratory primate welfare'' (table 1). Subsequently, 12 articles were analyzed.

This review focused on articles that met the following inclusion criteria: titles and abstracts directly related to topics of primates in scientific research, therapies in primates, ethical issues, promotion of animal welfare and legal protection. Only studies that addressed these issues centrally were selected, ensuring that the review remained within the defined scope.

Articles published in the last five years (2019-2024) were considered to ensure that the review included up-to-date data. The search was conducted in both Portuguese and English to ensure accessibility and understanding of the content. Articles related to experimental models in primates in scientific research, diseases in primate experimental models, and the welfare of primates in laboratory settings were included. The selected databases (PubMed, Scopus, and Web of Science) were used to ensure the quality and credibility of the scientific research. The selection of articles involved reading the titles, abstracts, and full texts, with duplicate studies being discarded. Exclusion criteria included articles published before 2019 to ensure the relevance of the data. Additionally, studies that utilized non-primate animal models, such as fish and rodents, were excluded as they were not relevant to the scope of this research.

The literature information on the proposed topics was described in brief summaries, and the findings from the literature were evaluated. The review of the articles was conducted according to the selected research topics, resulting in a total of 12 articles that met the inclusion criteria and were eligible to be discussed in this review.

3. RESULTS AND DISCUSSION

The results described in this literature review provide a comprehensive analysis of the use of non-human primates in scientific research, therapies, ethical issues, and the promotion of animal welfare, as well as aspects of legal protection, based on scientific articles retrieved from the PubMed, Scopus, and Web of Science databases, focusing on publications from the last five years.

Table 1 – Results found in the databases: Authors, 2024.

Database	Theme	Result
Pubmed	Experimental model in primates	402,111
	Primates in scientific research	669,342
	Diseases in primate experimental models	283,019
	Laboratory primate welfare	1,493
Scopus	Experimental model in primates	1,026
	Primates in scientific research	239
	Diseases in primate experimental models	532
	Laboratory primate welfare	5
Web of Science	Experimental model in primates	16
	Primates in scientific research	984
	Diseases in primate experimental models	31
	Laboratory primate welfare	5

The data demonstrate that there is a substantial amount of research involving primates, both in the areas of experimental models and general scientific research. The difference in numbers between PubMed and Scopus may reflect varying criteria among scientific journals and the number of articles per searched topic. The vast amount of research on this subject indicates significant interest in using primates to understand human diseases and develop new therapies.

3.1 Primates in Scientific Research

The clinical and histopathological effects in non-human primates (NHPs) exposed to supralethal doses of total or partial body irradiation (12 Gy) were evaluated, along with the potential protective actions of gamma-tocotrienol (GT3), a promising medical countermeasure (MCM) for radiation [1]. In the study on clinical and histopathological effects, the main objective was to explore and document the pathological consequences of these exposures using NHPs and assess the efficacy of GT3, which is currently under development [1]. In accordance with the 3Rs principles, the study revealed that such supralethal radiation exposures cause severe clinical and pathological injuries to major organ systems in NHPs [1].

According to a survey conducted by primate veterinarians, research primates may undergo surgical procedures, making effective pain management essential to ensure both animal welfare and the integrity of scientific data [6]. However, the research uncovered inconsistencies in pain management in primates and a general lack of objective tools for its assessment. These inconsistencies reflect gaps in the literature on primate pain, including limited pharmacokinetic studies and efficacy testing for common analgesics, as well as limited objective pain measures [6].

3.2 Neurodegenerative Diseases in Primates

Non-human primates (NHPs) are crucial animal models for studying complex human diseases, understanding biological functions, and evaluating the safety of new diagnostics and therapies intended for human use [7]. Due to their genetic, physiological, immunological, and developmental similarities to humans, they serve as important preclinical models for human health and disease [7]. Thus, non-human primates will continue to be essential for addressing key issues and providing predictive models in identifying the safety and efficacy of new diagnostics and therapies throughout human life [7].

Among neurodegenerative diseases, Parkinson's disease (PD) is a complex condition characterized by progressive motor deficiencies, including resting tremor, bradykinesia, limb rigidity, and postural instability, as well as a range of non-motor symptoms such as sleep disturbances, hyposmia, gastrointestinal dysfunction, autonomic dysfunction, and cognitive impairment [2]. Pathologically, the disease is marked by dopaminergic neuronal loss and the presence of Lewy bodies [2].

In recent years, researchers have focused on replicating the symptoms of human Parkinson's disease (PD) by establishing various experimental animal models, primarily through pharmacological agents and transgenic methods, to mimic relevant pathologies and identify effective treatments [2]. Over the past decades, substantial efforts have been dedicated to replicating the symptoms of human PD in animal models [2]. For a long time, Parkinson's disease was considered exclusive to humans. However, studies have shown early PD-like symptoms in aged macaques [8].

Additionally, significant synucleinopathy has been observed in certain aged non-human primates, with documented cases of naturally occurring PD in monkeys [9]. These findings highlight the significant potential of NHPs in PD research. Commonly used NHP models include macaques and baboons, with PD models established through neurotoxin induction or transgenic techniques.

Due to the lengthy experimental periods and the high labor and financial investments required to establish transgenic PD models in NHPs, chemically induced models are more frequently utilized [10]. MPTP-induced NHP models (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) have been widely employed in preclinical studies, with older monkeys showing greater susceptibility to infection compared to their younger counterparts [11].Some studies observed instability in older rhesus macaques following intramuscular injection of MPTP; however, subsequent adjustments led young rhesus macaques to exhibit motor symptoms, such as bradykinesia and resting tremor, as well as non-motor symptoms, such as gastrointestinal dysfunction and lethargy, when intramuscular MPTP injection was combined with intravenous MPTP injection over 18 weeks [12]. Therefore, when examining cognition and behavior related to PD, data obtained from NHP models provide more accurate insights into human PD [13].

3.3 Ethical Issues and Promotion of Animal Welfare

Despite growing ethical concerns, primates are still frequently used in invasive research, which involves bodily manipulations that cause pain or suffering and do not have a direct objective of improving animal welfare [14]. The use of non-human primates (NHPs) in such research raises serious welfare concerns, as their complex cognitive and emotional abilities make them particularly sensitive to the negative consequences of invasive procedures [14]. These investigations can significantly impact the physical and physiological well-being of NHPs, with long-term negative effects [14]. They may remember stressful experiences for many years and possibly anticipate future situations, amplifying the stress and pain experienced [14].

Additionally, NHPs have complex social lives with specific needs and requirements, making it challenging to provide adequate welfare conditions in a laboratory environment [14]. Research on the psychological and physiological well-being of animals in captivity has focused on investigating different types of social and structural enrichment [15]. As a result, cognitive enrichment has received less attention, despite its promising external validity, comparability, and applicability [15].

3.4 LEGAL PROTECTION

The legal protection of non-human primates generally relies on the principle of the 3Rs, although there is significant variation among countries in the practical implementation of this principle [14]. In the countries that are part of the European Union, animal research projects are only approved if they meet two standards that differ from those adopted in the United States. One of them requires a harm-benefit analysis to be carried out, as well as stipulating that a maximum level of pain and suffering imposed on the animals cannot be exceeded. In the US, on the other hand, although there is a similar warning, the federal laws and policies that legislate most government-funded research do not explicitly require the responsible bodies to conduct this analysis when approving protocols [16]. The pressure to enhance this legal protection mainly comes from animal advocacy organizations supported by public opinion, political groups within national institutions, and researchers working in ethics, philosophy, or alternative methods [14].

4. CONCLUSION

Primates play a crucial role in scientific research due to their similarities with humans, facilitating advances in various scientific fields. However, it is essential to balance scientific benefits with rigorous ethical considerations and efforts to improve the welfare of laboratory primates. The future of primate research must prioritize the reduction in the number of animals used and the development of alternative methods that can replace or complement current models. The findings of this review indicate that primates remain essential experimental models for research across diverse areas of knowledge, providing insights into human biology and contributing to the development of new therapies. However, their use in research faces significant challenges, particularly regarding ethical considerations due to their evolutionary proximity to humans. This necessitates a rigorous scientific justification and the implementation of measures to minimize animal suffering. This review also emphasizes the ongoing need to enhance the care and welfare of laboratory primates and the importance of developing new alternatives.

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3. The input prompt used was: ‘‘Translate the text from Portuguese to English, without altering the meaning of the sentences’’.

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