From In Vivo to In Silico:
The Role of Animal Models in Advancing Our Understanding of Brain Diseases

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Abstract

Animal models have played a critical role in advancing our understanding of brain diseases. In this essay, we discuss their advantages and limitations and examine two examples of successful advances in our understanding of brain diseases, including one case where they did not deliver the desired outcomes.

We then look to the future of neuroscience research, including the potential of using cell cultures and computational models in conjunction with animal models. We conclude by emphasising the ongoing importance of animal models in advancing our understanding of brain diseases.

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1 Introduction

Animal models have been invaluable tools in biomedical research, particularly in the field of neuroscience. Through the use of animal models, it is possible to delve into the complexity of our brains and uncover ways that diseases manifest themselves. In vitro, in vivo, and in silico research are some of the methods utilised in neuroscience research, as shown in Table 1.1. However, in vivo animal models provide a unique advantage in allowing researchers to study the entire organism in a controlled environment, where many variables can be controlled.

Method	Definition
In vitro	Research conducted using isolated biological components in a controlled environment, such as cell cultures or organoids.
In vivo	Research conducted using living organisms, often using animal models, to study the effects of a treatment or intervention.
In silico	Research conducted using computational models or simulations to predict the effects of interventions on biological systems.

Table 1.1: Comparison of In Vitro, In Vivo, and In Silico Research Methods.

The use of animal models is crucial in the study of diseases affecting the human brain. While we cannot use humans in every case due to ethical concerns, animal models allow us to study the progression of diseases in a way that is impossible with human subjects. In addition, researchers can use animal models to investigate disease mechanisms at the molecular, cellular, and systemic levels, which is difficult or impossible to do in humans since, for example, the modification of human genomes is not possible due to ethical and safety concerns.

Animal models have significantly advanced our understanding of many neurological disorders, such as Alzheimer's, Parkinson's, and stroke. They allow us to gain insight into the underlying mechanisms of these diseases, which can then lead to new therapies or treatments. For example, studies utilising mouse models have helped researchers better understand the role of genetics in Alzheimer's disease (Holtzman et al., 2011) and

Parkinson's (Hernandez et al., 2016). Additionally, animal models have been instrumental in providing insight into the effects of substances, such as the effect of prenatal alcohol consumption on the brain (Bisen et al., 2019).

Research with animal models is commonly utilised to assess the safety and effectiveness of potential treatments and drug therapies for neurological diseases, thus reducing the chances of unfavourable outcomes in human trials. This process involves obtaining various types of value from animal models, such as face value, predictive value, and construct value, to assist with translating research findings to humans. Additionally, researchers can now manipulate neuronal networks in model animals using new technologies such as optogenetics and chemogenetics, providing a better understanding of disease pathology.

However, it is important to note that animal models do have limitations. While they can provide valuable insight into disease mechanisms, they do not always translate perfectly to human disease. Moreover, there are ethical concerns surrounding the use of animals in research, which has led to the development of alternatives such as cell cultures and dish brains.

In conclusion, animal models have been instrumental in advancing our understanding and treatment of diseases, especially in the field of neuroscience. While they have limitations and ethical considerations, the ability to study the entire organism, generate genetically modified strains, and modify neuronal networks in controlled environments provides researchers with invaluable insight into disease mechanisms. Moreover, with the advent of new technologies and complementary methods, such as computational neuroscience and in vitro approaches, animal models can be combined with other techniques to help solve the mysteries of the human brain.

2 Advancements with Animal Models

3 Shortcomings of Animal Models

Animal studies have shown that NMDA receptor antagonists can reduce brain damage caused by stroke. However, clinical trials in humans have not been successful in replicating the same results. For example, the drug selfotel, which was effective in animal studies, failed to show a significant clinical benefit in a large human clinical trial.

Another example is the use of neuroprotective agents for the treatment of traumatic brain injury. Many neuroprotective agents have shown promise in animal studies, but clinical trials in humans have been largely unsuccessful. For example, the drug tirilazad was found to be effective in animal models of traumatic brain injury but did not show a significant clinical benefit in human clinical trials.

These examples highlight the importance of carefully evaluating the effectiveness of interventions in both animal models and humans and suggest that the translation of findings from animal models to humans is not always straightforward.

4 Combination of Different Research Methods

5 Conclusion

Bibliography

Bisen, S., Kakhniashvili, D., Johnson, D. L., & Bukiya, A. N. (2019). Proteomic Analysis of Baboon Cerebral Artery Reveals Potential Pathways of Damage by Prenatal Alcohol Exposure. *Molecular & cellular proteomics: MCP*, *18*(2), 294–307.

Hernandez, D. G., Reed, X., & Singleton, A. B. (2016). Genetics in Parkinson disease: Mendelian versus non-Mendelian inheritance. *Journal of Neurochemistry*, *139*(S1), 59–74. _eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1111/jnc.13593. URL   https://onlinelibrary.wiley.com/doi/abs/10.1111/jnc.13593   (Accessed at: 2023-02-13)

Holtzman, D. M., Morris, J. C., & Goate, A. M. (2011). Alzheimer's disease: the challenge of the second century. *Science Translational Medicine*, *3*(77), 77sr1.