Introduction

Understanding Through Animal Models

By Gal Yadid, PhD

Animal models in biomedical research provide an interactive, dynamic system that can be observed and manipulated experimentally in order to promote our understanding of a human condition or disease by elucidating the biological mechanisms underlying normal function and disease. Animal models allow researchers to test hypotheses about the causes and cures of a disorder and to develop effective therapies.

Animal models are commonly used in all areas of biomedical research and have contributed significantly to medical progress. For example, seven of the last 10 Nobel prizes in medicine have relied at least partly on animal models. Recent advances in the treatment of human disease have also been made using animal models. Prion proteins were first discovered in hamsters in 1982, leading to the further understanding of their nature and mechanism of action. Studies have used primate and rodent models of Alzheimer’s disease to test treatments that slow memory loss in patients with Alzheimer’s disease. Primate models have also paved the way to testing glial cell line-derived neurotrophic factor delivery to Parkinson’s disease patients. Finally, studies in rodents relating to cocaine self-administration have led to new possibilities for anti-craving medications.

The basic assumption in using an animal model is that there is a homology between the physiological and behavioral characteristics of different species. Animal models are most often judged by their demonstration of one or more of the following validities: face, predictive, construct, etiological, convergent (or concurrent), and discriminant.

It is generally believed that an animal model is stronger if it has demonstrated a wide sampling of the validities mentioned above. Predictive validity is particularly important if, presumably, the ultimate goal is to develop novel therapeutics to treat the human malady. However, the ultimate “proof” of the validity of an animal model for most researchers is the establishment of the therapeutic value of novel compounds that were developed based on a new understanding or treatment derived from the animal model.

This issue of CNS Spectrums covers progress toward the development of animal models of central nervous system (CNS) disorders. It presents new and exciting ideas and current issues in developing animal models of CNS disorders. In this issue, each of the articles addresses one of the many approaches that can be used to create an animal model of a CNS disorder. Interestingly, there is an inherent contradiction between novel and valid animal models. The validity of a truly novel animal model is somewhat difficult to evaluate because it may take several years to develop an animal model that shows high face, construct, and predictive validity. Fortunately, even without the establishment of all of the validities, a model may still contribute to an understanding of the disease.

Four different approaches to developing animal models (behavioral, pharmacologic, local gene delivery, and transgenic breeding) are presented in this issue for five different CNS disorders.

In the behavioral approach, animals are trained to elicit responses that are reminiscent of certain CNS illnesses. As an example of this approach, Eberhard Fuchs, PhD, puts forward social stress in tree shrews as an animal model of depression.

In the pharmacologic approach, animals are treated with either acute or chronic pharmacologic substances to elicit symptoms of a CNS disorder. David Eilam, PhD, and Henry Szechtman, PhD, suggest psychostimulant-induced behavior as an animal model of obsessive-compulsive disorder.

In the transgenic breeding approach, animals are genetically manipulated to induce symptoms of a CNS disorder. Animals (almost exclusively mice) receive genes from another organism into their genome. As such, Deby Van Dam, PhD, and colleagues present APP23 mice as a model of Alzheimer’s disease.

Finally, in the local gene delivery approach, which is related to both the pharmacologic and transgenic approaches, adult animals are infected with a gene that elicits symptoms of a CNS disorder. Matthew Maingay, MSc, and colleagues offer the overexpression of β-synuclein as a model of Parkinson’s disease as an illustration of this method.

Each of these methods of animal model approaches has its inherent advantages and disadvantages. Together, they provide researchers with a broad range of ways to study and analyze disease mechanisms and treatment.

REFERENCES