Animal Models for Evaluation of Antidepressant Activity: A Review

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***Abstract*—Depression is a common and serious psychiatric disorder that affects mood, behavior, and overall quality of life. It is one of the leading causes of disability worldwide and poses a major public health challenge. Preclinical evaluation using animal models plays a crucial role in understanding the neurobiological basis of depression and in screening potential antidepressant drugs before clinical use. Since depression cannot be fully reproduced in animals, different experimental models are used to mimic specific behavioral and neurochemical aspects of the disorder. This review discusses commonly used animal models for the evaluation of antidepressant activity, including behavioral despair models and stress-based models. Emphasis is given to their methodology, advantages, limitations, and relevance to human depression.**

***Index Terms*—Depression, Antidepressant drugs, Animal models, Forced swim test, Tail suspension test**

I. INTRODUCTION

Depression is a chronic mood disorder characterized by persistent sadness, loss of interest or pleasure, fatigue, sleep disturbances, and impaired cognitive function [1]. It affects millions of people worldwide and significantly reduces quality of life and work productivity [2]. The pathophysiology of depression is complex and involves disturbances in monoamine neurotransmitters such as serotonin, norepinephrine, and dopamine, along with neuroendocrine and stress-related mechanisms [3].

Although several classes of antidepressant drugs are available, many patients experience delayed onset of action or incomplete therapeutic response [4]. Therefore, there is a continuous need for the development of safer and more effective antidepressant agents. Experimental animal models are essential tools in antidepressant research, as they help in understanding disease mechanisms and evaluating drug efficacy before clinical trials [5].

II. RATIONALE FOR ANIMAL MODELS IN DEPRESSION

Animal models of depression are designed to reproduce certain features of human depressive disorders, such as behavioral despair, anhedonia, and stress-induced behavioral changes [6]. These models are widely used for screening antidepressant drugs and studying their mechanisms of action. A valid animal model should demonstrate face validity, construct validity, and predictive validity to ensure relevance to human depression [7].

III. ANIMAL MODELS FOR ANTIDEPRESSANT ACTIVITY

A. Forced Swim Test (FST)

The forced swim test is one of the most widely used behavioral models for evaluating antidepressant activity in rodents [8]. In this test, animals are placed in a cylinder filled with water from which escape is not possible. After initial escape-oriented activity, the animal adopts an immobile posture. The duration of immobility is considered an index of behavioral despair [9].

Antidepressant drugs reduce immobility time and increase active behaviors such as swimming or climbing. The forced swim test is simple, rapid, and sensitive to a wide range of antidepressant drugs,

making it suitable for routine screening [10]. However, it mainly reflects acute drug effects and may not fully represent chronic depression.

B. Tail Suspension Test (TST)

The tail suspension test is commonly used in mice to assess antidepressant activity [11]. In this model, mice are suspended by the tail, leading to periods of immobility after initial struggling. Antidepressant drugs significantly reduce immobility duration [12].

The test is easy to perform and requires minimal equipment. However, it is mainly applicable to mice and may be influenced by changes in motor activity [13].

C. Learned Helplessness Model

The learned helplessness model is based on exposure of animals to unavoidable and uncontrollable stress [14]. Animals subjected to repeated inescapable stress fail to escape when escape becomes possible, reflecting behavioral characteristics similar to human depression.

Chronic treatment with antidepressant drugs reverses helpless behavior in this model. Although it closely mimics stress-related depression, the model is time-consuming and requires careful ethical consideration [15].

D. Chronic Mild Stress (CMS) Model

The chronic mild stress model involves exposing animals to a variety of mild and unpredictable stressors over several weeks [16]. This model induces anhedonia, a core symptom of depression, commonly assessed by reduced preference for sweet solutions.

The CMS model has good face and construct validity and is particularly useful for evaluating the effects of chronic antidepressant treatment [17]. However, it is labor-intensive and requires strict standardization of experimental conditions.

IV. DISCUSSION

Animal models play a key role in antidepressant drug development. Behavioral despair models such as the forced swim test and tail suspension test are widely used for initial screening due to their simplicity and sensitivity [8,11]. Stress-based models like learned helplessness and chronic mild stress provide deeper insight into the pathophysiology of depression and long-term drug effects [15,17]. Selection of an appropriate model depends on study objectives, drug class, and available resources [5].

V. CONCLUSION

Animal models are indispensable tools for evaluating antidepressant activity and understanding depressive behavior. Each model has its own advantages and limitations, and no single model can fully represent human depression. Rational selection and proper application of experimental models improve the reliability of preclinical findings and support the development of effective antidepressant therapies [5,7].

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