Theranostics of
Brain, Spine & Neural Disorders
ISSN: 2641-8096

Juniper Publishers
key to the Researchers

Review Article
Volume 3 Issue 2 - May 2018
DOI: 10.19080/JOJS.2019.03.555609

Theranostics Brain,Spine & Neural Disord

A Practical Animal Model for Depression by Reserpine-Administered Mice

Ryan Greenwood[1], Jingjie Zhao[2], Brad Ludrick[1], Teresa Golden[1] and Ning Wu[1]*

[1]*Department of Biological Sciences, Southeastern Oklahoma State University, Durant, Oklahoma 74701, USA*

[2]*Department of Traditional Chinese Medicine, Beijing Friendship Hospital, Capital Medical University, Beijing, China*

Submission: May 11, 2018; **Published:** May 21, 2018

***Corresponding author:** Ning Wu, Department of Biological Sciences, Southeastern Oklahoma State University, Durant, Oklahoma 74701, USA, Email: nwu@se.edu

Abstract

Reserpine is a drug that was introduced in 1950 and is primarily used in the treatment of hypertension. However, studies began to arise showing supportive evidence that the chronic use of Reserpine has a serious side-effect of depression. This led researchers to use Reserpine administered in mice to produce a practical animal model for depression. This model has been used in numerous experiments to examine and compare the symptoms of depression in mice to those of humans, as well as determining the efficacy of certain anti-depressant medications. This study is a review of the methods in which this animal model for depression is used and how the functionality of this model has been implemented in recent studies.

Abbreviations: FST: Forced Swim Test; TST: Tail-Suspension Test; OFT: Open Field Test; RIH: Reserpine-Induced Hypothermia; SSRIs: Selective Serotonin Reuptake Inhibitors; MDD: Major Depressive Disorder; EPL: Extract from Paeonia Lactiflora; AD: Alzheimer Disease

Background

Depression is a serious health risk globally, and reports by the World Health Organization have predicted depression to be the leading global burden of diseases by 2030 [1]. Generally, depression is a disease affecting one's quality of life, and is commonly associated with dysfunctional mechanisms of neurotransmitters [2]. Common symptoms of depression include (1) feeling sad or anxious often; (2) feeling irritable or easily frustrated; (3) insomnia or excessive sleeping; (4) changes in eating habits or having no appetite; (5) trouble concentrating or hindered decision making; [6] feeling guilty or worthless; (7) decreased energy and fatigue; (8)thoughts of harming one's self; (9) suicidal contemplations [3].

Reserpine is a Rauwolfia indole alkaloid that acts as a sympatholytic and sedative agent and was once used as a primary treatment for hypertension [4,5]. However, evidence in research and clinical trials have shown that Reserpine has a serious side-effect, causing major depression after chronic use of the medication in a percentage of the drug's users, [6, 7]. Reserpine-mediated depression is thought to be caused by the depletion of monoamines in the brain, such as the catecholamine's adrenaline, dopamine, and nor epinephrine [8]. This is referred to the monoamine theory of depression and is supported by the numerous reports of depression after chronic use of Reserpine [9]. The mechanism of Reserpine is the irreversible binding to storage vesicles in monoaminergic neurons [10]. The vesicle can then leak, resulting in the seepage of transmitter into the cytoplasm where it is then destroyed by intraneuronal monoamine Oxidase. This causes a severe decrease or total depletion of active transmitter needed to be released at the synapse after depolarization [11,12].

The gathered evidence indicating Reserpine causes depression has led to the usage of the medication in animals, most commonly mice and rats, to produce a practical animal model for depression. This animal model for depression is a significant tool for studies examining the symptoms and pathological effects of depression in comparison to humans. This animal model is most commonly produced in hopes to resemble the neurochemistry of humans, shed insight on how the mechanisms of depression function, and analyze the efficacy of certain therapeutic drugs [13].

Methods for Measuring Depression-Like Behavior in Animal Models of Depression

The forced swim test (FST) or 'behavioral despair' test was developed by Porosity et al. in 1978 and is just one of several ways to help researchers measure depressive behavior in animal models [14]. The general FST is conducted by placing experimental animal in an inescapable cylinder containing 25°C water, for which the experimental animals must swim for 15 minutes. The experimental animals are then allowed to rest for 24 hours, and then repeat the FST after being administered Reserpine, in which the swim session is reduced to 5 minutes [15]. As time progresses during the FST, the experimental animals become more immobile, having only the

ability to keep their heads above the water or by floating. The time of immobility and the latency to the initial immobility period of the swim session are the primary dependent measures of the FST [16].Immobility periods are habitually increased in studies where experimental animals have been administered Reserpine, reflecting behavioral despair of the animal models.

The tail-suspension test (TST) is another method commonly used in measuring depression-like behavior in animal models. This procedure was first carried out by Steru et al. [17] and was conducted by suspending experimental animals by its tail with adhesive tape, then, while being acoustically and visually isolated, the immobility of the experimental animals was measured over a 6-minute duration. Similar to the FST, the measurement of the duration of immobility is used to indicate behavioral despair and is typically increased in animal models administered with Reserpine.

The open field test (OFT) is an observational method often used alongside the FST and TST methods. In contrast to the FST and TST, the OFT measures the locomotive and exploratory behavior of the test subjects, most commonly rodents. For this test, rodents are placed in an open and lit field large enough to move around in and are divided into peripheral and central units. Measurements are gathered within these units consisting of the locomotion and rearing behavior as well as the urination and defecation activity [18].

Studies of Reserpine have revealed the drugs ability to deplete the brain of serotonin. This affects the central nervous system similarly demonstrated by hypothermia [19]. This discovery led to the Reserpine-induced hypothermia (RIH) test to aid in the evaluation of depressive behavior. The purpose of the RIH test is to determine whether a drug has the ability to deplete the brain of serotonin, and therefore result in a decrease of body temperature. One study showed that mice being treated with Reserpine at a dose of 2.0mg/kg exhibited a significant increase in hypothermia compared to the control group [20].

Lastly, in another study, serotonin receptors 5-HT1A and 5-HT2A were both measured in a Western Blot analysis. These receptors are important to the effects of selective serotonin reuptake inhibitors (SSRIs). The activation of 5-HT1A or impediment of 5-HT2A receptors shows evidence of improving the effects of SSRIs. In this study, reserpinized experimental animals showed a decrease in the activation of 5-HT1A receptors and an increase in the 5-HT2A receptors [21]. Representing undesirable effects on SSRIs.

Current Studies Using Reserpine-Administered Mice as Animal Models for Depression

The Reserpine-administered mice as an animal model for depression are most commonly used in the efficacy of anti-depressant and anti-depressant-like effects. A study investigating the anti-depressant-like effects of ethanol extract from *Paeonia Lactiflora* (EPL) was able to collect clear evidence that EPL was successful in producing these effects. Supporting evidence was collected by revealing doses of EPL greatly decrease the immobility on certain tests such as the FST and TST. Other supporting tests were conducted such as the RIH test [22].

One study performed used Reserpine-induced Major depressive disorder (MDD) mice to determine whether the effects of MDD altered the expression of Alzheimer disease (AD) proteins, as they both commonly exhibit neuroinflammation and altered expression of neurotrophic factors. The Reserpine-treated test groups were used in comparison to the vehicle-treated groups and provided strong evidence that there is a pathological correlation between MDD and AD [23].

In another study, researchers were able to establish a fibromyalgia animal model by using the repeated use of Reserpine administration in mice. This repeated administration of Reserpine was effective in doing so as it diminished the number of biogenic amines such as dopamine and nor epinephrine, in areas deeply involved in pain signal processing. The study also represented a decrease in the FST, indicative of depressive behavior which is commonly acquired in patients with fibromyalgia. This animal model for fibromyalgia will allow researchers to obtain a better understanding of the disease and broadens the use of Reserpine-administered mice in different aspects other than depression [24].

Summary

Depression is rapidly increasing globally and is a great risk to a person's health and overall quality of life. The use of Reserpine-administered mice as a practical animal model for depression has consistently proven that it is a great tool for studies being conducted on depressive-like behavior. This animal model will continue to aid researchers in testing the efficacy of anti-depressants and anti-depressant-like components in hopes to discover improved treatments of depression disorders.

References

1. Ozerov AA, Bagmetova VV, Chernysheva Yu V, Tyurenkov I N (2016) Comparison of the Efficiency of Adeprophen and Antidepressants of Various Groups on the Model of Reserpine- Induced Depression in Rats. Bull Exp Biol Med 160(5): 649-652.
2. Cui J, Jiang L, Xiang H (2012) Ginsenoside Rb3 exerts antidepressant-like effects in several animal models. Journal of Psychopharmacology 26(5): 697-713.
3. (2015) US Department of Health and Human Services, National Institutes of Health, National Institute of Mental Health. NIMH Strategic Plan for Research (NIH Publication No. 02-2650).
4. Guo Z, Liu X, Huang H (2015) Kinetics and Thermodynamics of Reserpine Adsorption onto Strong Acidic Cationic Exchange Fiber. PLoS ONE 10(9): e0138619.
5. Holt Mary C (1961) Methoserpidine: A Non-Depressant Isomer of Reserpine. The British Medical Journal 2(5249): 415-418.
6. Freis Edward D (1954) Mental Depression in Hypertensive Patients Treated for Long Periods with Large Doses of Reserpine. New England Journal of Medicine 251(25): 1006-1008.
7. Leith NJ, Barrett RJ (1980) Effects of chronic amphetamine or reserpine on self-stimulation responding: Animal model of depression? Psychopharmacology 72(1): 9-15.

How to cite this article: Greenwood R, Zhao J, Ludrick B, Golden T, Wu N. A Practical Animal Model for Depression by Reserpine-Administered Mice. Theranostics Brain,Spine & Neural Disord. 2018; 3(2): 555609. DOI: 10.19080/JOJS.2019.03.555609

8. Gao ZY, Yang P, Huang QJ, Xu HY (2016) the influence of dizocilpine on the reserpine-induced behavioral and neurobiological changes in rats. Neuroscience Letters 614: 89-94.
9. Schildkraut JJ (1965) The catecholamine hypothesis of affective disorders: A review of supporting evidence. American Journal of Psychiatry122 (5): 509-522.
10. Minor TR (1990) Conditioned fear and neophobia following inescapable shock. Anim Learn Behav 18(2): 212-226.
11. Hanff TC, Furst SJ, Minor TR (2010) Biochemical and anatomical substrates of depression and sickness behavior. Isr J Psychiatry Relat Sci 47(1): 64-71.
12. (1981) Schwartz JZ Chemical basis of synaptic transmission: Vesicles store and release. In: Kandel ER, Schwartz JH, editors. Principles of neural science. London: E. Arnold: PP 113-115.
13. Urigüen L, Arteta D, DíezAlarcia R, Ferrer Alcón M, Díaz A, et al. (2008) Gene expression patterns in brain cortex of three different animal models of depression. Genes Brain and Behavior 7(6): 649-658.
14. Porsolt RD, Anton G, Blavet N, Jalfre M (1978) Behavioural despair in rats: a new model sensitive to antidepressant treatments. Eur J Pharmacol 47(4): 379-391.
15. Bogdanova OV, Kanekar S, D Anci KE, Renshaw PF(2013) Factors Influencing Behavior in the Forced Swim Test. Physiology behavior 118: 227-239.
16. Castagne V, Porsolt RD, Moser P (2009) Use of latency to immobility improves detection of antidepressant-like activity in the behavioral despair test in the mouse. Eur J Pharmacol. 616(1-3): 128-133.
17. Steru L, Chermat R, Thierry B, Simon P (1985) The tail suspension tests: A new method for screening antidepressants in mice. Psychopharmacology 85(3): 367-370.
18. Fuchs E, Flügge G (2006) Experimental animal models for the simulation of depression and anxiety. Dialogues in Clinical Neuroscience 8(3): 323-333.
19. Mahesh R, Jindal A, Gautam B, Bhatt S, Pandey D (2011) Evaluation of anti-depressant-like activity of linezolid, an oxazolidinone class derivative – An investigation using behavioral tests battery of depression. Biochemical and Biophysical Research Communications 409(4): 723-726.
20. Gao S, Cui YL, Yu CQ, Wang QS, Zhang Y (2013) Tetrandrine exerts antidepressant-like effects in animal models: Role of brain-derived neurotrophic factor. Behavioural Brain Research 238: 79-85.
21. Li S, Han J, Wang DS, Feng B, Deng YT, et al. (2016) Echinocystic acid reduces reserpine-induced pain/depression dyad in mice. Metabolic Brain Disease 31(2): 455-463.
22. Mao Q, Huang Z, Ip S, Che C (2008) Antidepressant-like effect of ethanol extract from Paeonia lactiflora in mice. Phytotherapy Research 22(11): 1496-1499.
23. Lee HR, Hwang IS, Kim JE, Choi SI, Lee YJ, et al. (2012) Altered expression of γ-secretase components in animal model of major depressive disorder induced by reserpine administration. Laboratory Animal Research 28(2): 109-114.
24. Nagakura Y, Oe T, Aoki T, Matsuoka N (2009) Biogenic amine depletion causes chronic muscular pain and tactile allodynia accompanied by depression: A putative animal model of fibromyalgia." PAIN 146(1-2): 26-33.

DOI: 10.19080/JOJS.2019.03.555609

How to cite this article: Greenwood R, Zhao J, Ludrick B, Golden T, Wu N. A Practical Animal Model for Depression by Reserpine-Administered Mice. Theranostics Brain,Spine & Neural Disord. 2018; 3(2): 555609. DOI: 10.19080/JOJS.2019.03.555609