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## VARIOUS BEHAVIORAL ANIMAL MODELS USED FOR SCHIZOPHRENIA

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# VARIOUS BEHAVIORAL ANIMAL MODELS USED FOR SCHIZOPHRENIA

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## ABSTRACT

**Background:** Schizophrenia is a mental disorder in which alteration of brain neurotransmitters take place and these alterations applicable for producing symptoms like positive, negative and cognitive. What if a person interprets actual reality abnormally? Is it psychosis or is it schizophrenia? Comprehensive search reveals that people with schizophrenia seem like they have lost contact with reality. Comprehensive search reveals that people with schizophrenia seem like they have lost contact with reality and remitting disorder associated with significant impairments in social, vocational functioning and shortened lifespan. Actually patients Patients with schizophrenia also suffer disproportionately from mood symptoms and substance abuse, and approximately 10% die from suicide. Diabetes, hyperlipidemia, obesity, cardiovascular disease, human immunodeficiency virus and hepatitis-c virus are common physical health problems seen in people suffering from Schizophrenia, complications of pregnancy and birth in females also plays role in building schizophrenia. Neurotransmitter hypothesis considered as imbalance of dopamine, serotonin, glutamate, NMDA, acetylcholine, adrenaline and GABA, whereas enzymatic hypothesis such as acetylcholinesterase, catechol-O-methyltransferase, monoamine oxidase, phosphodiesterase etc., are also involved. Antipsychotics agents are utilize in the treatment of schizophrenia and are proved to be effective in the management of hallucinations, delusions and thought disorders. This review also considered the behavioral animal models used for schizophrenia for evaluation of learning, construction, cognition, stress, hyperlocomotion and stereotypy activities for the diagnosis of schizophrenic symptoms.

**Objective:** Objective of this review is based on the study of various behavioral animal models used for schizophrenia and assessed the schizophrenic symptoms.

**Methods:** Various animal behavioral models used for the determining the schizophrenic symptoms, using the keywords animals behavioral models in schizophrenia or psychosis.

**Result:** Various animal behavioral models such as Actophotometer, Stereotype behaviors, Forced swimming test (FST), Passive avoidance test, Catatonia in rats, Foot-shock induced aggression and Swim induced grooming in mice were compiled in this review for easy learning or assessing behavioral parameters of schizophrenia.

**Conclusion:** In the previous clinical or preclinical studies symptoms like positive, negative, and cognitive are seen in schizophrenia affected people. Moreover, symptoms are assessed by conducting behavioral, biochemical and neurochemical estimation on rodent/human trial. Animal models have been based on the management of behavioral parameters believed to be involved in schizophrenia. This review provides a brief overview of behavioral animals models used for the diagnosis of schizophrenia.

**Keywords:** Schizophrenia, actophotometer, stereotype behaviors, forced swimming test (fst), passive avoidance test, catatonia in rats, foot-shock induced aggression and swim induced grooming.

## INTRODUCTION

Swiss psychiatrist Bleuler, describes schizophrenia as a syndrome of distorted perceptions and behaviors [1]. Schizophrenia is a debilitating psychiatric disorder that affects 1% of the worldwide population. Many researchers over the years had the general aim of finding a specific neurochemical deficiency in schizophrenia. Although, all the catecholamine's or neurotransmitters in the brain defective and/or altered neurotransmission systems in schizophrenia [2]. Although some insights into the

etiology of schizophrenia have been developed, an understanding of the illness on the molecular level remains elusive and it is a multifactorial neurodevelopmental disorder influenced by both genetic and environmental factors, such that monozygotic siblings of affected individuals show a 50–80% risk of developing the disorder [3]. In current research, brain diagnostic strategy such as molecular genetics, neuroanatomy, neurophysiology, brain imaging and psychopharmacology represent important avenues [4]. Animal models provide the opportunity

to decipher the relationships between the nervous system and animal behavior as they serve as obligatory tools for screening of drug tests [5]. An animal model is a non-human species used in medical research because it can mimic aspects of a disease found in humans. In animal model, the experimental influence that promotes behavioural, biochemical and neurochemical changes in schizophrenia [6].

#### **Actophotometer**

Actophotometer was used to measure locomotor activity. Each animal was placed in the activity chamber of the apparatus and total locomotor counts were stated in expressions of photo beam interruption during a time period of 10 min [7].

#### **Stereotype Behaviors**

Rearing is a stereotype vertical locomotor activity involving an animal standing on its hind limbs, while raising up with its forearms in the air or placed on the wall of the cage, indication of an increase in exploratory behavior, which is a measure of central nervous system excitation. Induced falling describe as number of falls on the floor. These stereotype behaviors were checked in animals for a total period of 10 minutes. The mouse was placed into a plastic cage (37x24x30cm) which was divided into quadrants by lines on the floor. Before start the experiment mouse allowed to explore the plastic cage for 30 minute. After the previous dose of drug stereotypic behaviours (falling; number of falls on the floor), (turning; number of turns around), (head bobbing; number of neck turn up-down and left-right), (weaving; number of grooming, rearing) was produced by mice. When performing this test, counting the total number of falling, turning, head dipping and weaving etc., are the stereotypic behaviours which were measured in each 10 minute at an interval of 10 minute over 60 minute [8].

#### **Forced Swimming Test (Fst)**

The FST is the most frequently used behavioral test for measuring depressive-like behavior in rodents. FST was used to amount the immobility period according. In this test, animal were forced to swim in the glass chamber (25x15x25cm) containing water up to the height of 15 cm ( $23 \pm 2^\circ\text{C}$ ). Acquisition of the state of immobility with minimum floating is considered as behavioral despair akin to depressive symptoms of psychosis. Mouse was placed for 2 min in the chamber for habituation and afterwards

immobility period was recorded for the next 4 min [9].

#### **Passive Avoidance Test**

Passive avoidance test is commonly used to measure the step down latency (SDL) which is a parameter to check the memory of small animals. Passive Avoidance task is a fear-aggravated test used to evaluate learning and memory in rodent models of CNS disorders. the grid floor. A Passive avoidance paradigm was used to measure the cognitive perspective of psychosis [10]. The model consists of a chamber (27x27x27cm), whose one wall is made of plexiglass, three walls made of wood, besides a grid floor with wooden platform. A 15W bulb was used to illuminate the chamber and 20V AC electric shocks were given to floor during the experiment. Experiment was performed into two learning sessions followed by one memory session. During the first learning session, animal was placed on wooden platform and when it stepped down on grid floor or all its four paws touched to grid at a time not exceed upto 60 sec, shocks was delivered for 15 sec. Next learning session was performed after an interval of 90 min, in which animals were free from shock. For evaluation of cognitive function of animals, memory session was considered; this memory session was performed on next day and the animal was observed for 300 sec and it was also noted that animals were not delivered shocks throughout the memory period in passive avoidance paradigm. [10].

#### **Catatonia In Rats**

Catatonia induced by neuroleptic drugs can also be measured by the PAW test [11], this measures the ability of rats to spontaneously withdraw its fore- and hind limbs. This test is performed 30 minutes after intraperitoneal injection of test drug. Male Wistar rats are placed on a Perspex platform (30x30cm with a height of 20 cm) containing two holes for the forelimbs (40 mm) and two for the hind limbs (50 mm) and a slit for the tail. The distance between the right and left forelimb holes is 15 mm and the distance between forelimb and hind limb holes is 55 mm. The rat is gently placed by placing the fore limbs and hind limbs in respective holes. In catatonic condition, whenever animal takes to withdraw one forelimb or one hind limb this behavior shows forelimb retraction time and the hind limb retraction time. Also calculate the average forelimb retraction time and hind limb retraction

time. Although, animal behaviour model shows increase in hind limb retraction time (associated with the antipsychotic potential) whereas, the increase in forelimb retraction time (associated with the potential to induce) extra pyramidal side effects [12].

#### **Foot-Shock Induced Aggression**

The test was described by Tedeschi *et al.*, for the detection of neuroleptics, positive effects with anxiolytics and other centrally effective drugs test in rodents, which were correlates with dopaminergic system [13]. This test was performed on mice; two mice are placed in a box (with a grid floor consisting of steel rods at a distance of 6 mm). This box consists of constant current shocker with an associated scrambler through which a constant current of 0.6 or 0.8 mA is supplied to the grid floor. The total numbers of rounds are recorded for each pair during the 3 minutes period via delivered 60- Hz current for 5 sec followed by 5 sec interval for 3 minutes. In this way, mice pair is individually dosed and tested without previous exposure. Completion of test, animal behavioral parameters are measured. The test substance or the standard drug is applied either parenterally 30 minutes before the test or orally 60 minutes before the test. The percentage inhibition of aggressive behavior is considered with respect to the control group. Neuroleptics such as haloperidol inhibit the aggressive behavior. This test is not specific for anti-psychotics, meanwhile it shows positive results with anti-anxiety drugs as well as other psychoactive agents in addition to neuroleptics [12].

#### **Swim Induced Grooming in Mice**

Grooming induced in mice after a period of swimming was potently blocked by neuroleptic in dose dependent manner and is mediated via dopaminergic systems [14]. Induced climbing, sniffing and swim-induced grooming test in rodents are widely used models for screening antipsychotic drugs. Swim induced grooming test was performed by placing each mice in swimming cylinders with cylinder 8x8x18cm dimensions and filled with water at temperature not exceeding than 32°C. They were then removed and dried with a towel for 30 seconds and placed immediately into Perspex boxes individually. The number and the total duration of grooming attempts were recorded over 15 min.

periods as described in the literature [15-16].

### **CONCLUSION**

Schizophrenia is a severe psychological sickness in which people interpret actuality abnormally. Comprehensive treatment entails a multi-modal approach, including psychopharmacology, psychosocial interventions, assistance with housing and financial sustenance etc., are utilize in the treatment of schizophrenia and are proved to be effective in the management of schizophrenic symptoms. This current article have to highlights a number of possible animals behavioral models such as actophotometer, stereotype behaviors, FST, passive avoidance test, catatonia in rats, foot-shock induced aggression and swim induced grooming in mice, which have been observed in individuals with schizophrenia. Animal models support us to elucidate complex mechanisms and provide a reasonably reliable platform to test the prospective of new substances. Emphasis is placed on the critical evaluation of currently available models because these models help to shape the direction of future research.

#### **Consent for Publication**

Not applicable.

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#### **Conflict of Interest**

The author declare no conflict of interest, financial or otherwise.

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