A COMPREHENSIVE REVIEW ON DIFFERENT EXPERIMENTAL MODELS TO SCREEN NOOTROPIC ACTIVITY

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ABSTRACT

Good memory power acts as a catalyst in all walks of life. Cognitive deficits, alone as developmental deficit, demand the use of memory enhancers to boost cognitive abilities. Till date many number of animal models are developed to assess the nootropic activity of the drug and there is great diversity in applications of these experimental models. A single model can be used to evaluate many pharmacological action of a drug. The present study is therefore focused on discussing some popular experimental models to assess memory enhancing activity and analysing the specific conditions in which particular animal model is indicated.

Keywords: Cognition, Nootropic, Pharmacological action

INTRODUCTION

Nootropics also called smart drugs or cognitive enhancers are drugs, supplements, or other substances that improve cognitive function, particularly executive functions, memory, creativity, or motivation, in healthy individuals[1]. Various animal models have played a major role in the history of modern drug development to assess memory enhancement and many methods have been applied which would provide important insight into the mechanism of human memory. Rodents like rats and mice are the principally used animals to study cognition and behaviour related studies. The present study is therefore focused on discussing such memory enhancing animal models like, Elevated plus maze, Open field, Passive avoidance, Lithium induced head twitches.

1. Elevated plus model (EPM): EPM is the most commonly employed animal behavioural model of anxiety and memory enhancing activity. Groups consist of 6 male rats for each dose is made and trained for 5 days. The drug is administered 30min before the assessment of parameters. The model is commonly employed for screening putative anxiolytics and the brain mechanisms of anxiety[2].

There is great diversity in applications of the elevated plus maze. To name a few,

1.Pre-screening of newly developed pharmacological agents for treatment of anxiety-related disorders can be carried out.

2. Elevated plus maze is recently extended to measure the long-term spatial memory in animals[3].

3. Mechanisms (e.g., GABA, glutamate, serotonin, hypothalamic − pituitary–adrenal axis neuro-modulators) underlying anxiety behaviour can be assessed.

2. Open field: The Open Field Maze was initially developed as a test to measure emotionality in rodents[1]. Groups consist of 6 male rats for each dose is made and training is given for 2-10 min during training session. The test session is performed after some interval and tested for memory. It is a model to test memory in a new environment without any clearly aversive or appetitive stimuli. A number of variables can be scored in the open field maze with most parameters involving different types of motor activity. Many behavioural tests of anxiety are based on the subject animal's body activity and locomotion[4].

Measurement of several parameters in an open field device allows differentiating between various types of sedative or stimulant drugs[5].

3. Passive avoidance (Pole climbing): This model is used to study cognitive functions, mainly a response to conditioned stimuli during learning and memory. Mice or rats of both the sexes are trained and test session is done after an interval of 24h (for long-term memory), less than 6h (for short-term memory), or up to 3min (for working memory). This is used to examine long term memory based on negative enforcement[3]. It is also used to study psychotropic drugs, novel amnesic drugs and drugs having tranquilizing activity which are known to influence learning and memory process by modulating neurotransmitter system[6].

4. Lithium induced head twitches: Head twitches induced by lithium chloride in rats constitute a useful model for quantifying the 5-HT (Serotonin receptor) activity in the brain and for the screening of potential antagonists at 5-HT receptors. 6 male rats in each trial group is treated with lithium carbonate (190mg/kg body weight I.P with distilled water) after 30min of drug administration and number of head twitches are counted for 60min. It has been indicated that an increase in serotonergic transmission in the median raphe of mid brain will interfere with learning acquisition and memory consolidation. This confirms anxiolytic activity of the drug[7]. If the drug has its action on neurotransmitters then it can be known through the model lithium induced head twitches[8].

DISCUSSION

Elevated plus-maze method is a useful model to measure memory as it does not require manipulation of appetitive behaviours such as food or water deprivation, since it is based on spontaneous behaviour and it does not require the use of noxious stimuli such as electric shock and swimming stress, since it is based on natural aversion.

This model has demerits like; it requires large numbers of animals and testing, although not require expensive equipment is labor intensive, so equally expensive[9].

Open field model is an experiment used to assay general loco motor activity levels and anxiety in rodents in scientific research and willingness to explore in rodents[10]. However, the extent to which behaviour in the open field measures anxiety is controversial as the results are usually not satisfactory when confronted directly with clinical syndromes[11].

Due to the idiopathic nature of anxiety, animal models have flaws that cannot be controlled. Because of this it is better to do

the OFT in conjuncture with other test such as the elevated plus maze[12].

The Passive Avoidance task is useful for evaluating the effect of novel chemical entities on learning and memory as well as studying the mechanisms involved in cognition[5]. This test procedure is employed in different modifications. One of the most common modifications is to induce amnesia in animals through electroconvulsive shock. The variability of this method is relatively high; therefore, it is necessary to test large groups of animals. Care should be taken while inducing electric shock and sound proof room is must for evaluation, Due to all these critical variables the results of different authors are difficult to compare[5].

Head twitches induced by lithium chloride in rats constitute a useful model for quantifying the 5-HT (Serotonin receptor) activity in the brain and for the screening of potential antagonists at 5-HT receptors[13].

Even-though above models have both positive and negative aspects, elevated plus maze is considered as reliable method as the procedure is simple, not time-consuming, and does not require expensive equipment and it possesses several advantages over existing tests such as radial-maze, Y- or T-maze, water-maze, passive avoidance, active avoidance etc: but if it has to be full proof then one has to study the model by inducing amnesia or cognition enhancing agents.

Many Ayurvedic drugs have been tried scientifically using above different models for example, Anxiolytic activity of *Vibhitaki phalamajja* (*Terminalia bellarica*) using Elevated plus maze model[14], CNS depressant activity of *Madayantika* (*Lawsonia inermis*) using Open field model[15], Memory enhancing activity of *Ashwattha* (*Ficus religiosa*) using Passive avoidance model[16], Nootropic activity of *Vidarikanda* (*Pueraria tuberosa*) using Lithium induced head twitches model[7].

CONCLUSION

1. Elevated plus maze is used to evaluate pharmacological agents like, memory enhancers and anxiolytics.

2. Open field is a behavioural model, used to measure both long term and short term memory along with evaluation of motor activity, sedatives and stimulant drugs.

3. Passive avoidance is mainly used to study cognitive function and also to evaluate psychotropic drugs, amnesic drugs.

4. Lithium induced head twitches model is used to study drug action on neuro transmitters.

Many other classical drugs like *Mahashatavari* (*Asparagussarmentosus*)[17], *Palandu* (*Alliumcepa*)[18], *Jeeraka* (*Carumcarvi*)[19]etc have classical reference as memory enhancers can be tested using these models.

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