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Research Article

Experimental Animal Models of Human Depression: Understanding the Mechanism of Anti-depressant Agents

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ABSTRACT

Experimental animal models are considered an important scientific tool used to understand the pathogenesis of depression and the mechanism of anti-depressant agents. Human depression is a unique and complex process of multifactorial etiologies. The research-based evidence suggested that a functional deficiency of norepinephrine (NE), 5-hydroxy tryptamine (5-HT), and other neurotransmitters result in depression. A mood alteration disease associated with neurotransmitter dysfunction or psychological stress. There are numerous experimental animal models available to screen antidepressant drugs, but their precise pathophysiology is not entirely well-known. The present review focused on depression assay studies that used a variety of experimental models, including acute stress models such as the forced swim test, models of prolonged physical or social stress such as social defeat, genetic models of secondary depression, and other experiments meant to clarify the mechanisms of antidepressant medications.

1. Introduction

Human affective disorder (mood disorder) is categorized into unipolar (depression/mania) and bipolar is mixed type (both depression and mania)[1]. The starting point of depression or mania is development of an episode. In the case of unipolar depression, there are 2-3 episodes developed in an average age but in bipolar cases number of episodes is more[2]. Unipolar disorders are prevalent, affecting roughly 20% of Bipolar illnesses, on the other hand, afflict both genders equally and impact only 1 to 2% of the population—roughly 10% of men and women. An estimated 280 million people in the world have depression, it is about 50% more common in men and women. Several causes exist for depressive episodes including drugs like reserpine, propranolol, and α-methyldopa etc. Apart from these, diseases like Parkinsonism, and myocardial infarction (MI) also play an important role in development of depressive episode[3]. Vitamin deficiency (majorly Vit-B1 deficiency) also contributes as major factors. On the basis of pathophysiology, a functional deficiency of NE (norepinephrine) and 5-HT (5- hydroxy tryptamine) at specific brain locations results in depression, associated with neurotransmitter dysfunction or psychological stress. Antidepressants are used in the treatment of a number of diseases, including Major Depressive Disorder (MDD), General Anxiety Disorder (GAD), and obsessive-compulsive disorder (OCD). Monoamine oxidase inhibitors (MAOIs), N-methyl-d-aspartic acid (NMDA) antagonists, serotonin partial agonist and reuptake inhibitors (SPARIs), serotonin antagonist and reuptake inhibitors (SARIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), norepinephrine dopamine reuptake inhibitors (NDRIs), and serotonin partial agonist and reuptake inhibitors (SPARIs) are some of the different classes of antidepressants[4,5]. The safety and tolerability profiles of antidepressant agents of different classes vary with their dose and duration, even though they are all thought to have comparable efficacy. Hence to understand these factors there is a need of preclinical research

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involves the use of animals[6]. In order to test new antidepressant candidate and to determine the mechanism

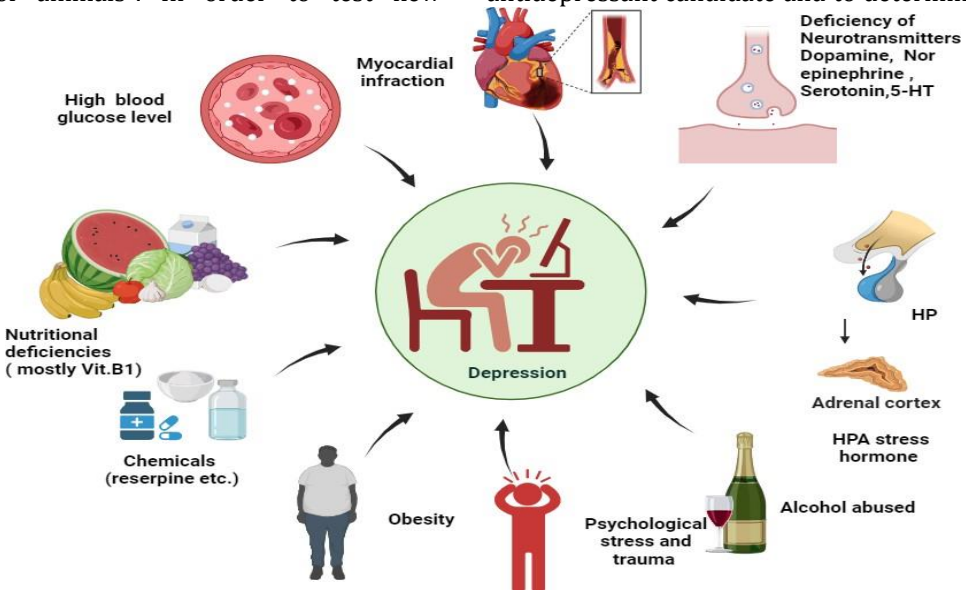

Figure1. Diagrammatic representation of pathophysiology of human depression

of action behind its effects, experimental animal models of depression are essential. There are many behavioural animal models exist those are used for the investigation of mechanisms of action of many antidepressant agents including Forced swim test, tail suspension test, and elevated zero- maze etc[7,8]. In this review, our efforts have been devoted to exploring the different animal models, instruments used with their pros and cons to understand the pharmacological mechanism behind them.

2. Pathophysiology of depression

The pathophysiology of human depression is very complex and not clear to understand. There is also no one theory exists that can account for all the signs and symptoms of depression. As per the scientific data revealed, the first type of depression is reactive depression that may be due to the unexpected happenings such as sudden death of beloved one etc[6]. Other factors contribute to precipitate depression include psychological stress and trauma, elevated blood sugar, nutritional deficiency, overactive Hypothalamic–Pituitary–Adrenal (HPA) stress hormone production etc. By considering the anatomical architecture and neurotransmitters involvement, large regions of the brain are innervated by most serotonergic, noradrenergic, and dopaminergic neurons, which are found in the brainstem and midbrain nuclei[8]. The monoamine-deficiency theory suggests that depression is caused by the depletion of neurotransmitters serotonin, norepinephrine, or dopamine in the central nervous system[9]. Serotonin is the most extensively studied neurotransmitter in depression, with evidence of abnormally reduced central serotonergic system function from tryptophan depletion. An individual that is more susceptible to depression experiences depressed symptoms as a result of this reduction, which could be caused by an increase in brain metabolism in the ventromedial prefrontal cortex and subcortical brain regions[10]. Multiple brain areas of patients with depression have been revealed to have abnormalities of serotonin receptors, specifically the serotonin-1A receptor. With decreased norepinephrine metabolism, increased tyrosine hydroxylase activity, and decreased norepinephrine transporter density in the locus coeruleus, the central noradrenergic system has been proposed to play a major role in the pathophysiology of depression(Figure 1)[11].

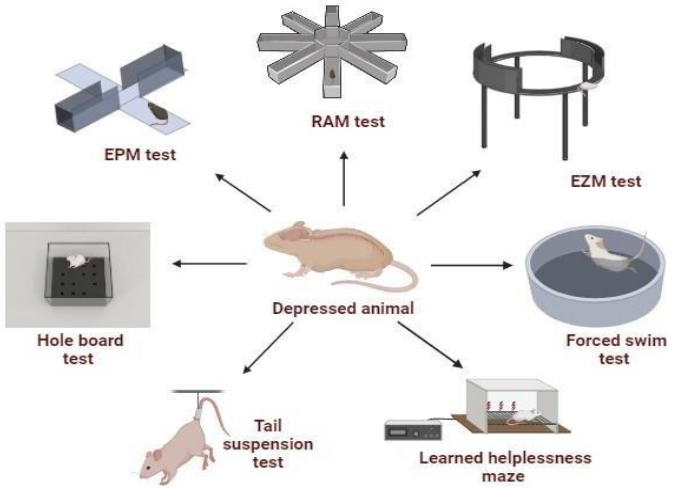

Figure 2. Different types of screening methods for antidepressant activity. EPM: Elevated plus maze, RAM: Radial arm maze, EZM: Elevated zero maze

The Elevated plus maze test is used as an experimental animal model for screening antidepressant activity. The Forced swim test is employed an experimental animal model to screen for antidepressant activity. The Tail suspension test serves as an experimental animal model for assessing antidepressant activity. The Learned helplessness test is utilized as an experimental animal model to evaluate antidepressant activity. The Elevated

zero maze test is employed as an experimental model for screening antidepressant activity. The Radial arm maze test is used as an experimental animal model for assessing antidepressant activity effects. The Hole board test is employed as an experimental animal model to screen for antidepressant activity (Table 1, Figure 2).

3. Elevated plus- maze test

The Elevated plus Maze (EPM) is a scientific tool used to assess anxiety/depression related behavior (Central nervous system CNS disorders) in rodent models (for rats and mice) [13]. The instrument was first introduced by Pellow (1985) for rats and later by Lister (1987) for mice[14,15]. The EPM apparatus consists of a plus-sign configuration ("+") made up of wood/acrylic/plywood etc. with four arms arranged in two opposite arms are open, and the other two opposite arms are enclosed by walls, forming closed arms. The entire apparatus is elevated above the ground, usually about 50-100 cm high, to induce a sense of vulnerability in rodents. Elevated Plus- maze for mice consists of two open arm (16×5cm) and two enclosed arms (16×5×12cm) with an open roof and is elevated to a height of 25cm and for rat, it consists of two open arm (50×40), two closed arm (50×10×40) and open roof with the 50cm high from the floor[16]. The floor of the maze is usually solid, providing a stable surface for the animals to walk on or move. The lighting conditions in the experimental room where the maze is located are crucial. Typically, the room is dimly lit to create an aversive environment for rodents, which encourages them to prefer enclosed spaces. To precisely quantify the behavior of rodents on the elevated plus maze, video tracking systems equipped with cameras placed above the maze can be used. These systems allow for automated tracking and analysis of parameters such as time spent in open and closed arms, number of entries into each arm, and distance traveled etc. Before testing, the maze is thoroughly cleaned to remove any olfactory cues left by previous subjects. Each animal is then placed individually onto the central platform, facing one of the closed arms as depicted in Figure 3, and allowed

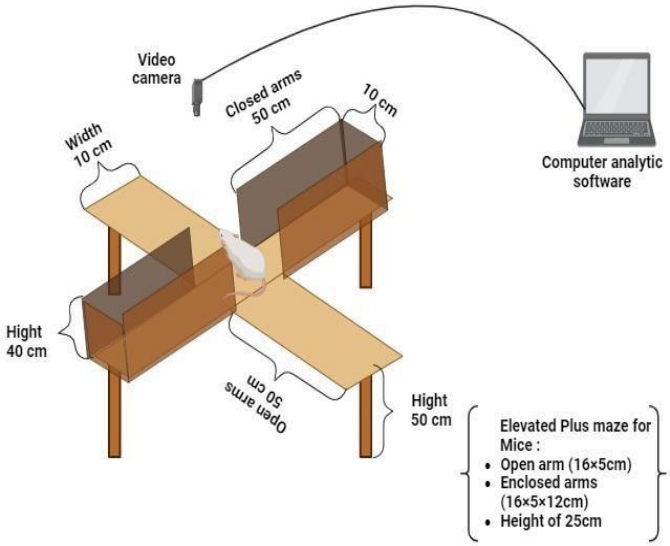

Figure 3. Elevated plus- maze test for rodent

to explore the maze for a predetermined period, typically 5-10 minutes. The ethological measures that can be observed in rodents in the maze are the number of rears, head dips, fecal boli, freezing or stretched attend postures etc to be taken into consideration. The test compound having serotonin, norepinephrine re- uptake inhibitory properties will prove as anti-depressant agent by elevating the levels of these neurotransmitters in the brain[17].

4. Forced swim test

The forced swim test (FST) is a widely used behavioral test for evaluating depressive-like behaviour in rodents (rats) and the efficacy of potential antidepressant agents. In this test, a rat is placed in a cylindrical container of water from which it cannot escape. The animal will initially make efforts to escape but will eventually exhibit immobility, which is considered to reflect a measure of "behavioral despair" or depressive-like behavior[18]. The test typically lasts around five to six minutes. For this experimental animal (rats) are randomly allocated into two groups i.e. test and standard and they are identified by fur marking with picric acid. Before initiation of experiment, the animals need to be trained for 1-2 days. On the day of experiment, the animal will be placed in a cylindrical container (25×12 × 25cm3) filled with water maintained with temperature 24°C to 30°C. The apparatus/container filled with 2/3rd water. The experimental animals allowed and forced to swim with container neither getting escape non getting the support via tail. Care should be taken to change the water for each animal forced to be swim because during swimming the fecal matter mix in water may cause depression to animal[19]. The test measures the time taken until the animal stops swimming and floats or performs only the necessary movements required to keep their head above water. Animal are placing in the container and time duration of observation are 4- 6 minutes as per

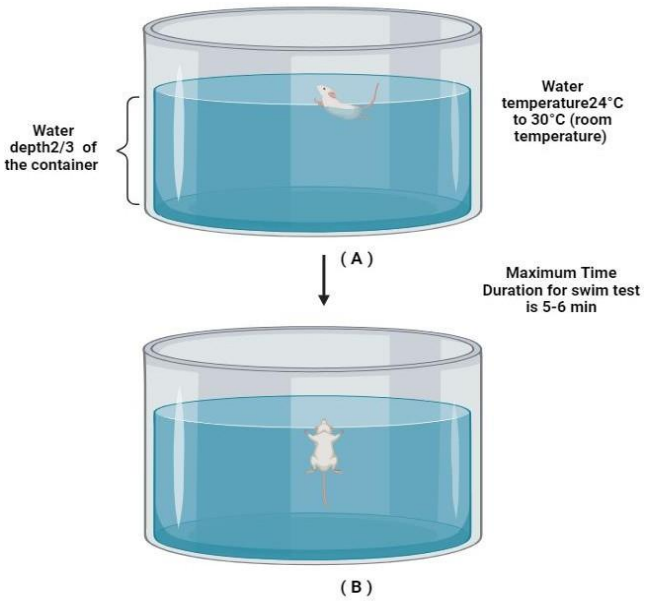

Figure 4. Swim test apparatus for rodents. **A:** Animal rigorously swim, **B:** Immobility due to depression

observations by different researchers. The investigator should observe and note the animal becomes immobile or has little movements to keep floating in the water. Measure the total immobility period during the six minutes test considered the animal immobile. After the test, animal is removed from the tank and allowed to dry by the help of either sun light or by electrical bulb. Then the animals returned to their home cage, where they are monitored for 10 minutes. The comparison will be made among the two groups and the data will analyze statistically (Figure 4)[20].

5. Tail suspension test

In 1985, Twain's introduced the first antidepressant test in tail suspension. The tail suspension test is based on the observation that an animal will eventually give up trying to escape when it is suspended from a height from which it cannot do so and will instead submit to the experimental conditions in a state of helplessness or despair. This phenomenon is used to evaluate newer antidepressant drug which are supposed to reduce this immobility period. In this test, the immobility period is directly record on the rotating drum (Figure 5) like subjective observations in case of other antidepressant evaluation test[21]. Critical assessment of tail suspension test conditions tape should be applied at the end of the tail and to the hook/suspension bar, and the experimenter should complete this process as quickly as possible to minimize the animal's stress[22]. The labor of manual scoring and various scoring criteria make obtaining robust data and comparisons across different studies challenging. The tail suspension test procedure involves weighing and numbering the animals, randomizes the animals according to body weight. The test and standard drugs are administered via oral gavage or any other suitable route[23]. Using sticky tape positioned about 1cm from the tip of the tail, the creatures are suspended from the edge over the tabletop (58cm). The writing pen to document the animal activity on the rotating drum should be on the other side of the lever. On the spinning drum that rotates at the proper

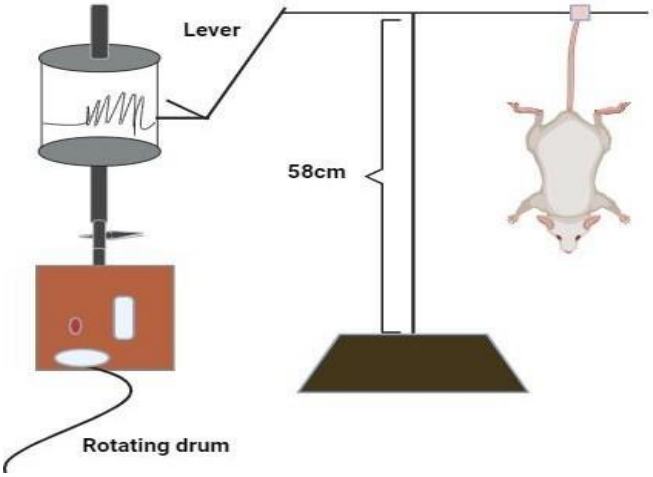

Figure 5. Tail suspension test apparatus for rodents

speed of 15 cm per minute[23], the length of the immobility period is recorded. When an animal is suspended motionless and passive, it is said to be immobile. The recording is done for a total of six minutes, and the rotational drum's trachings are used to compute the percentage immobility period. The result of both animal groups will be compared and statistically analyzed. The tail suspension test is a simple test having sensitivity to a wide range of drug doses. Disadvantage of tail suspension test includes, few specific mouse strains, such as C57BL/6, are prone to tail climbing during the test, which in turn render the test useless [25].

6. Learned helplessness test

Depression is said to have learned helplessness as one of its contributing factors. The animal exhibits this behavior in reaction to an unpredictable and unpleasant stressor; as a result, it will have impaired emotional expression, associative learning, and behavioral coping[25]. There is a connection between learned helplessness and the dorsal raphe nucleus, a region of the brainstem linked to serotonin and depression, and the ventromedial prefrontal cortex, a region of the brain that is critical for inhibiting emotional reactions. During such kind of stress, animals will essentially give up on trying to escape due to a sense of powerlessness. The test allows for the assessment of an individual's level of learning[27]. The learned helplessness maze, which consists of two equal-sized chambers divided by an acrylic wall, is the test apparatus employed. The shuttle box measures 50 cm in length, 15.5 cm in width, and 20 cm in height. A rectangular aperture, measuring 7.5 cm in height and 6 cm in width, was located in the center wall, 8 cm above the grid floor. The rat can leap from one side to the other through the opening in order to escape. The floor of each compartment is a separate grid made of 0.3-cm-diameter stainless steel rods placed 1.3 cm apart. The grid was lowered by the weight of

the animal[28]. A tiny switch that detects the animal's presence in that compartment is triggered when this occurs. Animals undergo a shock therapy for a predetermined number of days during the first phase. Only the control animal receiving shock will have an escape route available at this period; animals in the learned helplessness group will not. The treatment might last anywhere from minutes to an hour, after which the shock is typically randomly applied to simulate persistent symptoms. The animals are given a 24-hour period to recuperate following the first phase. Both sets of animals should have the escape mechanism placed into the chamber during the test phase and be subjected to shock once more. The control group will be familiar with operating the escape lever to enter the no-shock room. Even though there is a way out, the experimental group will just absorb the shock (Figure 6)[29].

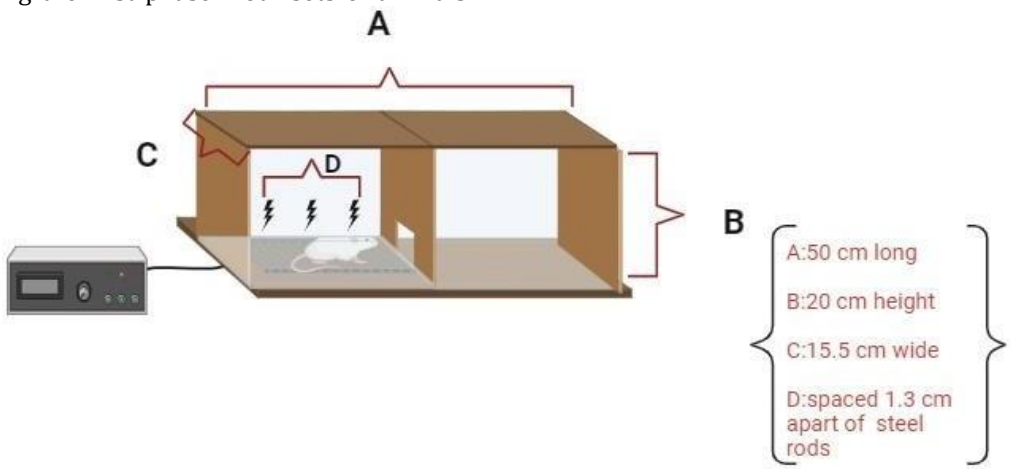

Figure 6. Learned helplessness test in rodent

7. Elevated zero- maze test

The elevated zero-maze is a variation on the elevated plus-maze that first described by Shepherd and colleagues in order to analyze medication effects, the elevated zero-maze design combines both conventional and cutting-edge ethological measurements[30]. About the description of an instrument. it is an annular platform with a diameter of 105 cm and a width of 10 cm that is split into two opposing open sections and two opposing closed sections (side walls 40 cm high). The exposed sections have 1 cm-tall borders. The apparatus is 50 centimeters above the ground and comprised just black-stained metal/acrylic pieces. Two opposite quadrants of the track are enclosed with walls that are typically around 20-30 cm in height. These closed arms provide a safe, enclosed environment that rodents tend to prefer due to their natural aversion to open spaces. The other two opposite quadrants of the track are left open without any walls or barriers. These open arms create an aversive environment for rodents due to the lack of protection and exposure to heights. The entire maze is elevated above the ground to induce a level of anxiety in the animals. The height can vary, but it's typically around 50-100 cm above the floor[31]. Lighting conditions can influence the behavior of rodents in the maze. Many studies used moderate lighting conditions, although some experiments may involve dim or bright lighting to investigate the effects of illumination on behavior. To track the movement of rodents within the maze accurately, a video tracking system can be employed. This system typically consists of a camera mounted above the maze and software for analyzing the recorded videos to measure various parameters such as time spent in open and closed arms, distance travelled, velocity, etc[32]. The maze should be placed in a quiet, isolated room to minimize external disturbances and to maintain consistent experimental conditions. Various evaluation parameter and behavioural activities are evaluated to study the potential of test compound under this model. This includes :(a) latency, or the first time all four paws were used to enter the open part from the closed part; (b) number of entries into the open part; (c) amount of time spent in the open arms; (d) number of line crossings in the open arms; (e) number of head dips over the edge of the platform; and (f) of stretch-attend posture (Figure 7)[33].

8. Radial arm maze

The radial arm maze developed by Olton and Samuelson (1976) allowing for the evaluation of treatment strategies for dysfunctional memory related to conditions

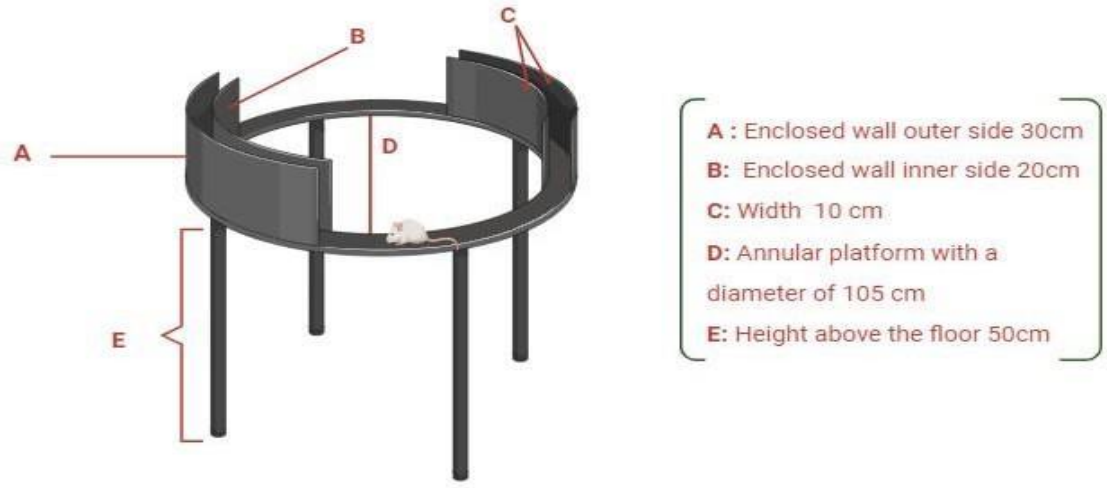

Figure 7. Elevated zero-maze test for rodent

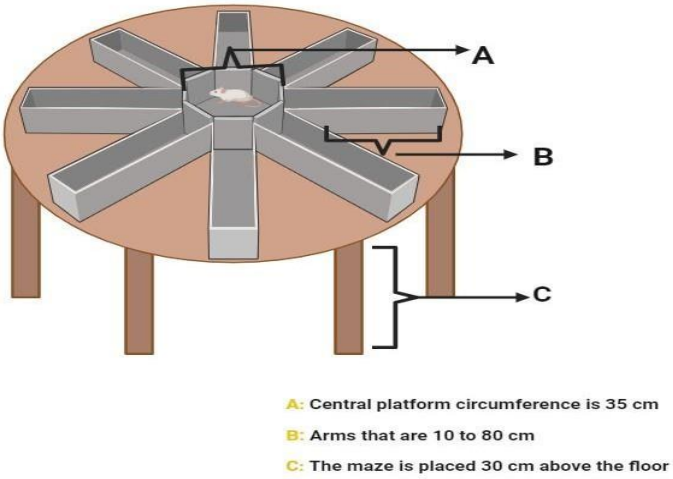

Figure 8. Radial arm maze test in rodents

such as depression[34]. The experimental area should have controlled lighting and environmental conditions to ensure consistency across trials[35]. To avoid stress and discomfort, the Illumination levels should be sufficient for the animals to explore the maze but not excessively bright. The maze is placed 30 cm above the floor, with eight arms that are 10 to 80 cm piece and a central platform that measured 35 cm in circumference. There is a meal cup at the end of each arm and some nutritional cereal is kept as a reinforcer. Alternatively, rewards can be placed at predetermined locations along the arms. Mice or rats are put in the middle compartment and given free reign to investigate every arm in the hopes of finding this prize. To prevent continually going into arms without a food reward during an experiment, the animal needs to be able to recall which arms it has been visited. Video cameras (optional) placed above the maze are used to monitor the behavior of the animals during the experiment. These cameras record the movement of the animals as they navigate through the maze. The use of the doors is all lowered when the animal is placed on the center hub at the start of the procedure, and all of the doors are simultaneously opened to let the rat freely select its arms[36]. When the animal visits each of the eight arms or spends ten minutes in the maze, the procedure is finished. Re-entry is counted as an error, while entry into an arm that the animal has not visited before is recorded as a correct response. The trial maze performance index is determined by counting the number of right answers before to making the first mistake, or the number of initial correct answers (Figure 8)[37].

9. Hole bored test

Rats' propensity to poke their noses or snouts through

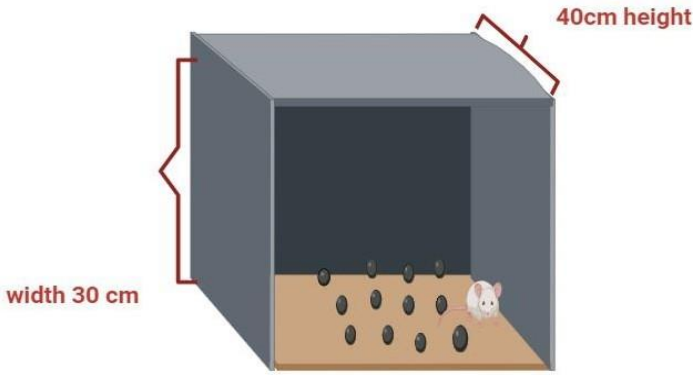

Figure 9. Hole bored test in rodent

holes has been measured using hole- boards also known as head-dipping, is a common prepotent action that has been demonstrated to be highly responsive to the effects of drugs[38]. The hole-board test, initially presented by Boissier and Simon (1962, 1964)[39], offers a straightforward technique to understand an animal's reaction, emotionality, anxiety, and/or stress response to an unusual setting. The size, shape etc. of hole board test can vary[40]. A circular hole-board with eight holes spaced around the sides has been used whereas in another study researchers used a hole-board with 16 round-shaped holes in the bottom of the experimental arena. The dimensions of the hole- board model is also varying, with different studies using a 40 cm x 40 cm x 30 cm apparatus[41]. The animal is kept in an arena with holes organized in a regular pattern on the floor for the length of the experiment, and the frequency and duration of spontaneously triggered hole-poking activity are recorded throughout this brief period of time. Additionally, the test offers a straightforward way to evaluate other related activities such grooming, raising, and disturbance. Additionally, the exam offers a straightforward way to evaluate other related behaviors, like grooming. The application of the hole-board from this viewpoint is predicated on the idea that animals' behavior in unfamiliar situations is the product of a conflict between their exploration and retreat tendencies.

So, an elevated rate of worry causes head-dipping to diminish, and a low level of anxiety causes head-dipping to increase. Depending on the behavior that is being measured, the hole board test can be altered. For instance, one animal is put in the device for five minutes to detect uneasiness, after which it is taken out of it. After receiving an anxiolytic injection, another animal is put within the device and watched. Nowadays, the hole board test is utilized as a neophilia test in numerous behavioral pharmacology domains (Figure 9)[42].

Table 1. Different type of antidepressant screening method with their modifications

Screening method	Reference	Year	Method	Output of the different generation voice modification ofthe method
Elevated plus maze	Handley and Mithani	1984	The authors have investigated an elevated X-maze with alternating open and enclosed arms a model for the evaluation of fear-induced behaviour.	The α1-adrenoceptor antagonists' prazosin and thymoxamine, enhanced the proportion of open arm entries at low doses[42].
Table 1. Continued				
	Pellow et al.	1985	The authors have investigated considering a proportionally larger apparatus. The +-maze consisted of two open arms, 50 x 10 cm, and two enclosed arms, 50 x 10 x 40 cm, with an open roof.	Extensive pharmacological, physiological, and behavioral validation of the EPM as an animal test of anxiety in rats[43].
	Lister	1987	The authors have given a typical rat maze has four arms arranged as a plus and is commonly elevated. The maze has two open arms (30 x 5cm) and two closed arms (30 x 5 x 15cm high walls) radiating from a central square (5 x 5cm). The floor of the maze is made of black (or gray).	There was also a significant ($p < 0.05$) decrease in the duration of grooming in the elevated plus maze test for the cooked beans and serotonin precursor fed group when compared to the control. Thus, chronic consumption of cooked beans diet may decrease anxiety and fear related behavior[15].
	Montgomery	1955	Authors has modification of an elevated maze with four arms arranged to form a plus shape.	Recording and analyzing the behavior of the very first rats authors got an inverse relation, with more intense exploratory behavior obtained with the lower edges (5 and 10 cm) and less exploratory behavior with the higher edges (20 and 40 cm transparent)[44].
Forced swim test	Wallach and Hedley	1979	The authors have evaluation forced to swim inside a verticals Plexiglas cylinder (height: 40 cm. diameter: 18 cm, containing 15 cm of water maintained at 25 °C).	Positive results with antihistamines[45].
	Buckett e t al.	1982	Modification of the despair swim test in mice involving a small water wheel set in a water tank	In contrast, methamphetamine, caffeine, and scopolamine reduced the duration of immobility not only during the first 5 min but also the next 15 or 25 min without prolonging the escape- directed behaviour but by increasing general motor activity[46].

	Giardina and Ebert	1989	The authors have used in this method 2000-ml beakers of containing 1400-ml of tap water at room temperature are gives animal to depressed like symptoms.	Captopril, an angiotensin II converting enzyme (ACE) inhibitor, was evaluated for potential antidepressive activity on the forced swim-induced behavioral despair (immobility) test in mice[47].
	Nishimura	1988, 1989, 1993	The authors have evaluation of the modification of the forced swim test using straw suspension in the water tank.	There were no differences in immobility during either rope- or straw- suspension[48].
	Hata et al.	1995	The authors have used cylindrical glass container 45-cm height, 28-cm diameter. Which contained tap water to a depth of 35 cm. for the evolution of depression like activity.	These data are consistent with emerging evidence that corticosterone may play a paradoxical antidepressive effect[49].
Tail suspension test	Steru et al.	1985	The method is based on the observation that a mouse suspended by the tail shows alternate periods of agitation and immobility.	Diazepam increases the duration of immobility[24,50].
	Chermat et al.	1986	In the tail suspension test (TST), authors have evaluation the rat is suspended by the tail for 6 min during which the animal shows periods of agitation and immobility.	Desipramine decreased the duration of immobility[51].
	Porsolt et al. and Steru et al.	1987, 1987	Authors has specially developed computerized device automatically measures the duration of immobility of 6 mice at one time and at the same time provides a measure of the energy expended by each animal, the power of the movements.	Recommended the use of the automated tail suspension test for the primary screening of psychotropic agents[52].
Learned helplessness test	Overmier and Seligman,	1967, 1976	Animals exposed to inescapable and unavoidable electric	Found that prior exposure to controllable shock[53].
	Maier, an d Seligman		Shocks in one situation later fail to escape shock in a different situation when escape is possible.	Immunizes the organism against the deleterious effects of exposure to uncontrollable aversive events[54].
	Sherman et al., Martin et al. Christensen and Geoffroy Tejedor del Real et al.	1979, 1986, 1991	Gives potential animal model of depression.	Inhibition of the uptake of biogenic amines was found to be the main mechanism of action resulting in downregulation of β- receptors[55,56].
	Vaccheri et al.	1984	Authors has used an apparatus with a lever to be pressed to interrupt the shock.	Desipramine (imipramine) and haloperidol were employed in each test as a standard antidepressant and neuroleptic[57].
	Porsolt et al.	1990	Used shuttle boxes for escape.	In Porsolt's test, dimethyl imipramine, imipramine, and amitriptyline decreased immobility time in stressed and control rats in a comparable way[58].
	Simiand et al.	1992	Used shuttle boxes for escape.	Potentiation of yohimbine toxicity and reversal of learned helplessness[59].

Table 1. Continued

	Curzon et al.	1992	Described a rat model of depression.	Tianeptine decreased the availability of 5- HT to receptors[60].
Elevated zero maze	Shepherd et al.	1994	These modifications include increasing arm length, using transparent walls, incorporating infrared sensors, and implementing video tracking systems.	Benzodiazepine anxiolytics, diazepam (0.125-0.5 mg/kg) and chlordiazepoxide (0.5-2.0 mg/kg) significantly increased the percentage of time spent in the open quadrants (% TO) and the frequency of head dips over the edge of the platform (HDIPS), and reduced the frequency of stretched attend postures (SAP) from the closed to open quadrants[61].
Radial arm maze	Olton et al.	1978 1979	The authors have used the radial arm maze is composed of a central platform with arms radiating from it like spokes of a wheel. A short edge (2 cm high) along the side of each arms helps the rat stay on the arm and not fall off the maze. A barrier between the arms, next to the central platform, is often used to prevent the rat from jumping directly from one arm to the next, forcing him to go to the central platform before making another choice. Evaluation of depression like activity.	Their outcome supports the hypothesis that the memory characteristics of tasks are the major factors influencing the magnitude of the impairment exhibited by rats with damage to the hippocampal system[62,63].
	Buresova et al.	1985	Authors has investigated the aversively motivated maze was developed by locating an 8-arm maze with 40x40x 12 cm channels was inserted into a circular tank (120 cm in diameter, 60 cm high) filled 30 cm deep with 25°C opaque water.	Obtained in the radial water maze indicate that spatial working memory can store not only locations of food but also, of the available safe places[64].
	Kesner et al.	1980, 1986	The first maze was used for the 8-arm maze task and second maze used has used for the adjacent-arm task and the place learning task and the third maze has used an elevated (80 cm from the floor) 12-arm radial maze,	CN-lesioned animals were profoundly impaired on retention of the egocentric tasks[63,65].

			painted white	
Hole board test	Smith et al.	1982	Modification involved altering the dimensions of the holes and adjusting the parameters for assessing exploratory behavior in rodents.	Analysis of agonists of the brain benzodiazepine binding site[66].

10. Conclusion

This systematic review studied a number of screening methods in relation to the models' height, shape, and size as well as how to start the study's methodology. The findings display the metrics that investigators have endeavored to quantify within their research study models. Numerous authors have used the screening procedure and their modification to study antidepressant animal models after doing a critical assessment of the base model. It is expected that the animal model studies summarized in this review will be helpful to the recent generation scientists and cause further research in the field of antidepressant screening of new compounds.

Declarations

Competing interests

The authors declare no conflicts of interest.

Authors' contributions

All authors have checked the ethical concerns such as plagiarism, misconduct, fabricated or false data consent to publish double publication and/ or submission redundancy.

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Ethical considerations

The authors declare that this manuscript is original and is not being considered elsewhere for publication. Other ethical issues, including consent to publish, misconduct, fabrication of data, and redundancy, have been checked by the authors.

Availability of data and materials

All data are collected from published studies and are available in the present article.

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