International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 7(1): January-February 2017

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Original Article……!!!**

Received: 13-02-2017; Revised: 18-02-2017; Accepted: 19-02-2017

COMMON ANIMAL MODEL FOR ANXIETY AND DEPRESSANT

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Keywords:

Animal Model, Anxiety, Depression, Common Animal Model, Reason to Have Common Animal Model

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ABSTRACT

Anxiety and depression arevery common psychotic disorders which are highly observed in the young generation and very much common in women than in men. According to the world health organization depression will be the second leading cause of disability in 2020 and he last not the least anxiety will be the fourth leading disability.Major depressive and anxiety disorder has lifetime prevalence i.e. 10 and 20% across genders. The treatment for the both the condition is possible but they interfere with the treatment to each other and they have the common symptoms too. The research on both the disorder is very high but during treatment they interfere with each other. In research many animal models are used. For the study of depression and anxiety common animal model are used due to many reason such as symptoms, treatment process and last not the least the chronic anxiety leads to the depression which show the symptoms of anxiety and depression both in a patient.This review article includes common animal models that are used for both depression and anxiety.

INTRODUCTION

A psychiatric disease is that which have a genetic component or, in other word quantitative genetics, genetic variation explains best behavioural variation [1]. The number is less for the common adult psychotic conditions, schizophrenia and manic depressive psychosis is common disorders in young generation, but it is still the largest known contributor to the disease aetiology [2]. Attempts made to find the genetic variants have responsible because popular research i.e. endeavours, pursued with apparently resistant to failure, but we can say remarkably small progress made till now [3]. In which the Animal models are the backbone for preclinical research on the different Central Nervous System disorder such as psychiatric disorders, and these both are employed as screening tools for novel therapeutic agents and for studies on underlying mechanisms [4-11]. More than enough animal models are used for anxiety and depression, in which some are based on physiological (e.g., hyperthermia) or endocrine (e.g., plasma corticosterone) responses. The vast majority are behavioural in nature. Depression and anxiety are the widely spread across the different age and social groups, and it is also the part of genetically determined disorder [13, 14]. Twice in women as in men, major depressive and anxiety disorder has lifetime prevalence i.e. 10 and 20% across genders [13-15].

ANXIETY

Anxiety is disorder experience by all of us with time to time [17].Many people related it with their feeling, tense, uncertain, fearful thought, going into hospital, attending an interview or starting a new job. Anxiety and fear are normal emotions with great adaptive value that is having the long evolutionary process, but sometime fear occurs in very high specific threats and the source of anxious behaviour is undefined or unknown. It may be of 2 types: SHORT-TERM ANXIETY and SEVERE ANXIETY [16].

Symptoms: Anxiety cause many sensations in your body as it is preparing us for the danger. These sensations are called the “alarm reaction”, which takes place in our body naturally at the condition of anxiety [19]. ALARM SYSTEM (THE “FIGHT-FLIGHT-FREEZE” RESPONSE) HAS BEEN ACTIVATED. Other symptoms are:

- Sweating
- Rapid heartbeat and rapid breathing
- Nausea and stomach upset
- Feeling dizzy or lightheaded
- Tight or painful chest
- Numbness and tingling sensations
- Choking sensations
- Hot and cold flashes [18,20]

PERSONS OF NOTE WITH ANXIETY:

Anthony Hopkins (actor), Barbra Streisand (singer), Abraham Lincoln (president) David Bowie (singer) Edvard Munch (artist) Eric Clapton (musician) Johnny Depp (actor) Nicholas Cage (actor) Nicole Kidman (actress) OprahWinfrey (host) Oprah Winfrey (host) Sigmund Freud (psychiatrist) and Sir Isaac Newton (scientist)

DEPRESSION

Depression is a serious medical condition in which a person feels very sad, hopeless, and unimportant and sometime the person is unable to live a life in a normal way [28]. The 6th century Indian philosopher and thinker AdiShankaracharya has said that "It is dispassion towards the ephemeral and connection with the eternal that brings true joy" [21,29]. Depression is a psychiatric disorder which is very poorly understood in the neurobiology. Depression, also termed as Major Depressive Disorder (MDD) [26], According to estimation by World Health Organization, depression will be the second leading cause of disability in 2020 [22]. Recent epidemiological studies indicate that severe forms of depression affect 2-5% of the population worldwide, and up to 20% are affected by milder forms of this disease [24].

Symptoms: The symptoms are daily seen at least 2 weeks. Many recent studies support that stressful events correlate with an increased vulnerability for depression which is just a hypothesis [27].

- Depressed or irritable mood,
- Decreased interest or loss of pleasure,
- Weight gain or loss,
- Insomnia or hypersomnia,
- Psychomotor retardation or agitation,
- Fatigue or loss of energy,
- Feelings of worthlessness or inappropriate guilt,
- Diminished ability to think or concentrate,
- Gender stressful life events,
- Recurrent thoughts of death and suicide.[23,25]

PERSONS OF NOTE WITH DEPRESSION

Woody Allen (film director), Ingmar Bergman (film director), Albert Camus (writer), Jim Carrey (actor), Sheryl Crow (musician), Fyodor Dostoevsky (writer), Vincent Van Gogh (painter), Ernest Hemingway (writer), Abraham Lincoln (16th President of US), Martin Luther (priest and theologian), Michelangelo (painter and sculptor), Isaac Newton (physicist), Friedrich Nietzsche (philosopher), Mark Twain (writer).

ANIMAL MODEL

A model organism is a non-human species that is highly used in recent years for to understand particular biological phenomena, with the expectation that discoveries made in the organism model will provide in-sight into the working of other organisms. Model organisms are in vivo models that are widely used in research human disease when human experimentation would be unfeasible or unethical. This strategy is made possible by the common descent of all living organisms and the conservation of metabolic and developmental pathways and genetic material over the course of evolution. Studying model organisms can be informative, but care must be taken when extrapolating from one organism to another [30].

Considerations in Choosing an Animal Model

- Adequate discrimination (data extra palatable to target species),
- Adequate fidelity (necessary anatomic structures, biochemical pathways, etc.),
- Good literature base; historical usage (i.e., accepted animal model),
- Readily available to other researchers,
- Genetic and microbiological characterization,
- Sufficient size for obtaining necessary samples (blood, urine, biopsies, etc.) and substance administration,
- Accommodation in existing animal facilities (caging, environmental controls, exercise and environmental enrichments),
- Experience/training of animal care staff,
- Experience/training of research staff,
- Tractable; trainable,
- Low cost (purchase; maintenance),
- Good reproductive performance,
- Minimal indigenous disease (or ability to control),
- Ethical considerations,
- Public relations implications. [31]

REASON TO HAVE COMMON ANIMAL MODELS

Psychologists are for taking care of the mental health in terms of specific disorders; the truth is that mental health is not always so black and white. Relationships between different psychological disorders can make complicated to diagnose, and it was experienced that more than one disorder is occur at the time (known as "comorbidity."). Two of the most common disorders in the world are anxiety and depression, and both of them have their own sub-disorders type, but they are chemically and technically different disorder, but they share a lot of common symptoms which affected the

misguidance and treatment for the disorder. It is very common to suffer from both the anxiety and depression at the same time, especially seen if you are suffering from severe anxiety. The anxiety comes first, and its impact on life leads to the depression and depressive symptoms [33].

"Even more than the depression, it was my anxiety and agitation that became the defining symptoms of my illness. Like epileptic seizures, a series of frenzied anxiety attacks would descend upon me without warning. My body was possessed by a chaotic, demonic force which led to my shaking, pacing and violently hitting myself across the chest or in the head. This self-flagellation seemed to provide a physical outlet for my invisible torment, as if I were letting steam out of a pressure cooker." ~ Douglas Bloch, M.A., author of "Healing from Depression" [35].

There are still many similarities between the two conditions, and remember that in some cases one can cause the other. The similar physical symptoms include:

- Nausea and stomach issues.
- Aches and pains for no apparent reason.
- Headaches [33]

The both anxiety and depression, is treatable. There have countless studies proving that those willing to commit to a treatment will find their conditions lessened or eliminated. The problem is that: Both anxiety and depression change your way of thinking, so that you often feel as though they're untreatable. Anxiety and depression require long term treatments. They won't have immediate results, both will have their own or same setbacks. There are two circumstances under which an anxiety patient may need specific help for depression. Due to these common symptoms or the common way of treatment and recovery leads to the have the common animal model for the drug research [34].

COMMON ANIMAL MODEL FOR ANXIETY AND DEPRESSION

OPEN FIELD TEST

The open field apparatus was a soundproof box with an uncovered square box (40 × 40 × 45 cm) inside. The inside area of the apparatus was black, and testing was conducted under dim light. The rat was placed in the area with its head toward the inside of the box and allowed to behave freely for 10 min. During the test, rearing times and face-washing times were counted by the experimenters, while other data, including total distance and time in the centre square, were analysed by the motion tracking system. After each trial, the rat was returned to its home cage, and the square box was cleaned with 75% ethanol and dried with an air drier. [25]

GELLAR'S SEIFTER TEST AND VOGEL CONFLICT TEST

The conflict test was firstly developed by Geller &Seifter [30] and later modified by Vogel, [30] and shows a high predictive value for classical anxiolytic drugs. In the Geller Seifter test, rats deprived of food for 24 hours are trained to press a lever and obtain a sugar-sweetened drink at variable intervals

(the non-punished component). In the test session, a signalling stimulus (such as a tone or a light) is introduced, indicating now that the lever-press behavior will always yield a reward but, at the same time, will be punished by an electric shock, producing a conflict between drinking the palatable water and receiving the shocks. In the control condition, the animal's tendency to press the lever decreases, whereas anxiolytic drugs show an anti-conflict effect, increasing the probability of punished responses. This effect is not due to antinociception, since is not observed after treatment with opioid agonists such as morphine. Psycho-stimulant drugs such as amphetamine alsofail to produce this effect. [32] Some years after the introduction of this model, Leaf & Muller [32] reported that shocks suppress the licking behavior of water-deprived rats. However, these researchers did not test usual anxiolytic drugs, an experiment that was later performed by U.S. researcher John Vogel in 1971[30].Vogel introduced a more simplified test, in which animals were deprived of water for 24 hours and briefly trained to find a bottle of water in an experimental box. On the next day (after another 24- hour period of water deprivation), the animals are re- exposed to the same box, which contains a stainless steel grid floor. The contact of the animal with the bottle spout and the grid floor closes an electrical circuit controlled by a sensor. After each 20 licks at the bottle of water, the animal receives a mild shock (0.5 mA) [29]. In this model, anxiolytic drugs also show anti-conflict properties, inducing an increase in the number of punished licks. Similar to the Geller–Seifter procedure, control experiments to avoid any drug effect in nociception and thirst should be performed. Even though both models described above have a good predictive value for benzodiazepines and barbiturates, the VCT also responds to some non-anxiolytic drugs, producing false-negative results.[32] Moreover, antidepressants produce inconsistent results in these models. Chronic treatment with tricyclic antidepressants and monoamine oxidase inhibitors, such as imipramine and phenelzine respectively, increases punished responses, but the serotonin reuptake inhibitor (SSRI) fluoxetine does not. [Chronic administration of the partial 5HT1A agonist buspirone also produces anti- conflict effects in rats, [35 and 34]but not in mice. [30] In comparison to the Geller–Seifter test, the VCT has the advantage of avoiding a prolonged training period. However, despite good predictive value regarding classical anxiolytics, these tests are susceptible to interference from several variables, such as hunger, thirst, pain, learning and memory, which can sometimes hinder interpretation of the results.

ELEVATED PLUS MAZE

The most employed animal model of anxiety and depression in current practice was first proposed by Handley &Mithani [35] and further validated by Fileet al. [36] the apparatus is raised above floor level, and is composed of two enclosed arms opposed perpendicularly by two open arms. The test is based on the natural tendency of rodents to explore novel environments and their innate avoidance of unprotected, bright, and elevated places (represented by the open arms). Confinement to the open arms induces physiological signs of stress (increased defecation and corticosterone levels), [36]

whereas exposure to classical anxiolytic or depression drugs, which increases the exploration of these arms [36]. The basal activity of the animals in the EPM is affected by several factors, such as housing conditions, lighting levels, circadian cycle variations, prior handling or stress exposure, and familiarity with the maze. For instance, individual housing increases anxiety or depression in rats but decreases it in mice, probably due to distinct social organization patterns between the species, while prior stress exposure markedly increases anxiety or depression. Moreover, re-exposure to the EPM results in marked reductions in open arm exploratory behavior and can totally abolish the effect [37-39]. In addition, the presence of the experimenter in the same room can also interfere with the results. Regarding the different variables that can be recorded in a 5-min EPM session, studies employing factor analysis suggested that the enclosed arm entries can be used as an uncontaminated measure of locomotors activity, while percentage of entries and time spent in the open arms constitute the primary anxiety index [36, 37, and 39].In addition to these classical measures, different groups have proposed the evaluation of other ethological variables, such as risk assessment of the open arms and head dipping in these arms, to increase the sensitivity of this model [40].

THE HOLE-BOARD TEST

The hole-board consists of a square arena with a number of holes in the floor that the rodents can explore by poking their heads.The test is based on this latterbehavior, named head dipping [43, 44] which has been validated as a measure of depression and anxiety [43]. The number of head-dips is assumed to be inversely proportional to the anxiety state and directly proportional to the depression [44]. Drug effects on this test, however, can be influenced by the familiarity of the animal with the test environment [46, 45] in mice a biphasic effect on exploratory head dipping, with lower doses increasing and higher doses decreasing this behaviour [45].

LIGHT/DARK BOX

The light-dark exploration test was developed before the EPM test by Crawley & Goodwin in the early 1980s [47]. Similar to the EPM, this animal model is based on the innate aversion of rodents to places with bright light. During a 5-min session, animals are allowed to freely explore a novel environment composed of two different compartments: protected (dark) and unprotected (lit). In rodents, this model generates an inherent conflict between their exploratory drive and their avoidance of the lit compartment [48, 47]. Treatment with anxiolytic drugs such as benzodiazepines increases the time spent in the lit compartment as well as the number of transitions between the two areas [48]. In this test, as in others that measure exploratory activity, particular attention should be given to drug- or genetic-induced changes in basal loco motor activity or novelty-seeking behavior (e.g., amphetamine treatment), since they could produce false positive results.

HYPONEOPHAGIA-BASED MODEL: NOVELTY SUPPRESSED FEEDING TEST

The first report of Hyponeophagia in rodents, i.e., the suppression of feeding generated by the increase in anxiety-like states of animals exposed to a novel environment, was made in 1934 by Hall [49]. In 1988, Bondoff et al [50] validated the novelty suppressed feeding (NSF) test. In this model, animals deprived of food for 24 hours are exposed to a transparent box consisting of a sawdust-covered floor, a central platform holding a single pellet of chow, and focused lighting. The latency for the animal to reach the centre of the box and initiate food intake is measured, being directly correlated with anxiety levels. Thus, this model creates a conflict between the natural tendency to feed after food-deprivation and the ethologic aversion of novel, brightly lit and central places. In this test it is also important to control for any drug-induced changes in food intake, which is usually done by measuring this variable in the animals' home cages [51]. In the NSF, acute and chronic administration of diazepam induces an anxiolytic-like effect, represented by a decrease in the latency to onset of eating [52]. Furthermore, in the case of antidepressants, the model exhibits good predictability, since it responds only to chronic treatment (minimum of 2 weeks), mimicking the time course required for the therapeutic effects of these drugs in humans. Due to this characteristic, the NSF is often employed after the chronic unpredictable stress procedure (where animals are exposed to daily different stressors for, at least, 14 days), which increases anxiety- like behaviours, to evaluate the anxiolytic and antidepressant properties of chronic treatments [52, 50]. Although it involves hunger, this test is well accepted since it does not require painful procedures or previous training.

SOCIAL DEFEAT STRESS

The social defeat stress (SDS) model was initially proposed by Klaus Miczec [53]. The SDS protocol consists of the introduction of a single mouse (known as the intruder) in the home cage of a resident male mouse (known as the aggressor) [53-57]. During the test, behaviours related to confrontation of the intruder mouse by the resident aggressor are recorded. The time spent by an intruder mouse in social defeat posture induced by the presence of an aggressor is computed throughout five trials by a blind observer. Defeat posture is identified by the followed criteria: immobility (four paws on ground, oriented toward the aggressor), escape (escaping from the aggressor), crouching (four paws on ground, not oriented toward aggressor), or defensive upright stance (standing erect with forepaws extended) [55]. The procedure can be used in acute or chronic stress protocols [56-58].

CHORIC MILD STRESS

The chronic unpredictable stress (CUS) model has been widely used to induce persisting stress-related behavioural changes in rodents [59]. It consists of randomly presenting different stressors to the rodents on a daily basis. This scheme prevents the stress adaptation process observed in other models of chronic stress [60]. In this model, animals are exposed for 2 to 5 weeks to a wide range of stressors, including foot shocks, restraint stress, light- dark cycle reversal, unpleasant noises, changes in the

home cage (removal of sawdust, replacement of sawdust with water, heating (37°C) or cooling (4°C) of the home cage). After several days of exposure to this regimen, the animals exhibit a gradually increased HPA axis sensitivity and a decrease in responses to pleasant stimuli, without; however, any change in exploratory activity [61]. This protocol has good face validity and seems to represent the stressors faced by humans in everyday life more realistically. Moreover, it has excellent predictive validity, since repeated treatment with antidepressants (fluoxetine, desipramine, or imipramine) is able to reverse the behavioural effects induced by this model [60].

FEAR POTENTIAL STARTLE

Fear conditioning is a form of Pavlovian conditioning that involves learning the association of a neutral CS, such as a light, tone, or setting, with an aversive stimulus (US), such as an electric shock. Re-exposure to the CS will activate a conditioned fear response which resembles the responses that occur in the presence of danger [64, 65] Conditioning learning can be elicited in several species, including humans [66, 63]. The defensive responses elicited by the CS in animals are characterized by freezing (complete immobility except as required for breathing), reflex expression (characterized by fear-potentiated startle), and autonomic (increase in heart rate and in the mean arterial pressure) and endocrine (stress-related hormone release) responses [65-69]. Fear conditioning models involve the encoding of traumatic memories, representing a psychological stress without physical stimuli [67, 69]. They have been associated with a vulnerability to phobic fears and other anxiety-related disorders, such as panic disorder (PD), agoraphobia, and posttraumatic stress disorder (PTSD) [71, 72]. In this model, administration of anxiolytic drugs immediately before the pairing of CS and US (during the memory acquisition process) affects the formation of conditioned learning. If administration occurs before the re-exposure to CS, it will affect fear and anxiety expression acquired during the conditioning. The drug could also affect extinction of the conditioned response, where a new learning process (that the CS no longer predicts the occurrence of the UCS) occurs after repeated exposure to a CS in the absence of the US [73]. Systemic administration of benzodiazepines or SSRIs reduces the freezing behavior observed during the expression of conditioned fear [74-76]. This is in agreement with clinical findings indicating that they are effective for the treatment of anxiety disorders [73]. However, in contrast to their clinical effects, SSRIs are effective after acuteadministration in this model [77, 78]. Li et al.,[79] however, showed that chronic treatment with SSRIs induces a greater attenuation of conditioned emotional responses after repeated rather than acute administration [79] In addition, several other factors can influence the effects of SSRIs, including the timing of drug administration, the kind of CS stimulus, and the intervals between acquisition and expression of conditioned fear [70, 80].

ELECTRIC FOOT SHOCK INDUCED STRESS

This protocol is very similar to the pre-test session described in fear conditioning-based models. Rodents are very susceptible to mild shocks, exhibiting a remark- able stress response after foot shock delivery. The protocol consists of placing rodents in a chamber with a metal grid floor connect to a shock generator. After a habituation period, animals receive mild (05-2 mA), brief (1-2 s duration) foot shocks. Like other stress protocols, electric foot shocks can be combined with anxiety tests [82, 81].

EXPLORATION OF NOVEL OBJECTS

The Novel Object Recognition (NOR) task is used to evaluate cognition, particularly recognition memory, in rodent models of CNS disorders. This test is based on the spontaneous tendency of rodents to spend more time exploring a novel object than a familiar one. The choice to explore the novel object reflects the use of learning and recognition memory. The Novel Object Recognition task is conducted in an open field arena with two different kinds of objects. Both objects are generally consistent in height and volume, but are different in shape and appearance. During habituation, the animals are allowed to explore an empty arena. Twenty-four hours after habituation, the animals are exposed to the familiar arena with two identical objects placed at an equal distance. The next day, the mice are allowed to explore the open field in the presence of the familiar object and a novel object to test long-term recognition memory. The time spent exploring each object and the discrimination index percentage is recorded. This test is useful for assessing impaired cognitive ability in transgenic strains of mice and evaluating novel chemical entities for their effect on cognition [149].

OLFACTORY BULBECTONY

Bilateral olfactory bulbectony (OB) results in endocrine, behavioural, immune system and neurotransmitter changes that mimic many of the symptoms seen in human patients with major depression [83]. The rat olfactory system forms a part of the limbic region, which includes the amygdala and hippocampus. These are responsible for functions such as memory and emotion, and are known to have altered morphology and activity in patients with depression. After OB, there is a marked degeneration of neurons in the olfactory bulb, but also in other areas such as the hippocampus, cortex, amygdala, locus ceruleus, and raphe nuclei. In all likelihood, these focal brain changes lead to the dysfunction in serotonergic and noradrenergic systems that are observed after bulbectony [85]. With regards to behavioural parameters in animals with OB, there is an increase in cannibalism and exploratory and locomotorsbehavior, as well as a decrease in sexual activity and behavioural and cognitive anhedonia deficits. Cellular level studies have also observed a reduction in the number of synapses and dendritic arborisation in the hippocampal and cortical neurons. Furthermore, reductions were found in the concentrations of serotonin and norepinephrine in the brains of rodents subjected to OB [84]. Changes in the immune system are quite evident in these

animals. Studies have also reported that many of thesechanges, both behavioural and cellular, are reversed by several classes of antidepressants used in the clinic [85]. With both behavioural changes and changes in neurotransmitters and in the immune system occurring after OB, we can conclude that this may be a good animal model of depression, since it has both face and construct validity. Moreover, different classes of therapeutically effective antidepressants reverse the behavioural and molecular changes caused by OB, thus showing that this model presents predictive validity. Chronic, but not acute, administration of antidepressants largely corrects most of the behavioural, endocrine, immune, and neurotransmitter changes that occur following bulbectony. Thus, the olfactory bulbectomized rat is not only a model for detecting antidepressant activity but also one for exploring the inter-relationships between these systems, which are also dysfunctional in patients with major depression [84].

INCLINED SCREEN RETENTION TEST

The method of Allmark and Bachinski (1949) [150] using an inclined screen was originally developed for testing curare-like agents. Later on, it has been used by many authors (e. g. Randall et al 1961) [151] for testing compounds for muscle relaxant activity. The principle of an inclined plane has been used by Ther, Vogel and Werner (1959) for differentiating neuroleptics from other centrally active drugs. Rivlin and Tator (1977) also used an inclined plane to assess skeletal muscle relaxation. The plane consists of two rectangular plywood boards connected at one end by a hinge. One board is the base; the other is the movable inclined plane. Two plywood side panels with degrees marked on their surface are fixed on the base. A rubber mat with ridges 0.2 cm in height is fixed to the inclined plane which is set at 65 degrees [152]. Male mice (Charles River strain) with a body weight between 20 and 30 g are used. The test compound or the standard are administered to groups of 10 mice either i.p. or S.C. or orally. Thirty, 60 and 90 min thereafter, the mice are placed at the upper part of the inclined plane and are given 30 sec to hang on or to fall off. The peak time is determined as the time at which a compound produces the maximum performance deficit. At this time interval, a range of doses is tested using 10 animals per group [153].

TABULAR FORM OF COMMON MODEL USED FOR ANXIETY AND DEPRESSION

NAME OF THE MODEL	OBSERVATION	TIME DURATION	ANIMAL USED	REASON FOR USING AS COMMON MODEL		MODIFICATION	REFERENCE
				ANXIETY	*DEPRESSENT*		
Open Field Test	Defecations/urinations number and duration; total distance travelled; distance in the inner area; number of squares crossed in the inner area; distance in the outer area; self-grooming latency; self-grooming duration; self-grooming frequency; latency to	10 min	Rodent	Ethologically relevant conflict or conditioned behaviour.	Investigate the symptomatology and pathophysiology	Exploration of novel objects in open field	Colman.A.M (2001) "open field test"A dictionary of psychology.encyclopedia.com.

	leave the central area						
Gellar's SeifterTest	Response-contingent electric shock	1hour	Rats	Raise the conflict rates as rat is in irritable mood.	Decreased the conflict rates as the rat is depressed.	Vogel conflict test Putative animal model	Geller i. The acquisition and extinction of conditioned suppression as a function of the base-line reinforce. J Exp anal behaves. 1960; 3:235-40. 39 Vogel jr, beer b, cloddy de. A simple and reliable conflict procedure for testing anti-anxiety agents. Psychopharmacologi cal. 1971; 21:1-7.
Elevated Plus Maze	Latency to leave the centre; total arms entries (4 paws criterion); enclosed arms entries; open arms entries (4 paws) and rears (2 paws); time spent in the open arms; time spent in the enclosed arms; open arms entries; time spent in the open arms; head dips defecations; urinations; self-grooming latency; self-grooming duration; self-grooming frequency; central platform crossings and time spent.	5 min	Rodents	Increase in the open-arm time as showing endophenotype behaviour.	Increase in the closed-arm time as rat is irritated and need calm area.	Y-shaped apparatus, zero maze, T- shaped apparatus	Pellow s, Chopin p, file se, Briley m. Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. J neuroscience methods. 1985; 14:149–167.
The Hole-Board Test	Head dipping activity; latency number, duration; defecations, urinations, total distance travelled/squares crossed, distance/squares crossed in the inner area, distance in the outer area, self-grooming, rears	5-15 min	Rodents and rabbits	Decreases in the number and duration of head-dips, and an increase in the latency to head-dipping as rat are in fear condition.	Increase in the number and duration of head-dips, and an decrease in the latency to head-dipping as rat is upset.	Modified hole board (mHR) paradigm	Takeda, h.; studio, m.; Matsumiya, t. (1998). "Changes in head-dipping behavior in the hole-board test reflect the anxiogenic and/or anxiolytic state in mice". European journal of pharmacology 350 (1): 21–29. Doi: 10.1016/s0014-2999(98)00223-4. Pmid 9683010
Light/Dark Box	Light box entries number, time spent, rears number, duration of light box rears, latency of the first rear and entry vertical activity in the light box, urinations, defecations, grooming.	10 min	Mice	Duration of time spent in bright-space show anxiety.	Duration of time spent in dark- space show depression.	marmoset (Callithrixjacchus)	Crawley J, Goodwin FK. Preliminary report of a simple animal behavior model for the anxiolytic effects of benzodiazepines. Pharmacol-BiochemBehav. 1980; 13:167-70.
Exploration Of Novel Objects	Number of approached and contacts, duration of contacts, latency of the first approach/contact.	10 min,	Rodents	Behavioural despair for exploration	Decreased interest for exploration	Exploration of novel objects in open field	Baxter MG. "I've seen it all before": explaining age-related impairments in object recognition.

							Theoretical Comment on Burke et al. (2010) BehavNeurosci. 2010; 124:706–709. Doi: 10.1037/a0021029.
HyponeophagiaBased Model: Novelty Suppressed Feeding Test	Latency to start eating novel food, first touch to the novel food.	15-20 minute	Rodents	In anxiety measuring the latency of an animal to approach and eat a familiar food in an aversive environment	In depression approach and eat a familiar food in an aversive environment	Neurogenesis-dependentsuppressed feeding test	Cryan JF, Sweeney FF. The age of anxiety: role of animal models of anxiolytic action in drug discovery. Br J Pharmacology. 2011; 164:1129- 61.
Inclined Screen Retention Test	Time spent on the screen (falling latency); urinations, defecations	30 sec	Male mice	Diminished ability to think or concentrate, Deficits in working and spatial memory	Distractibility, behavior easily disrupted by irrelevant stimuli	Instead of an inclined wooden board, an inclined screen has been used	Allmark MG, Bachinski WM (1949) A method of assay for curare Using rats. J. Am. Pharm. Ass 38:43–45
Olfactory Bulbectony	Behavioural hyper locomotion in the open field aggression	10-20 min	Rodents	Diminished think or concentrate power	Neuro-degeneration	----------	Song, C. and Leonard, B.E. (2005) The olfactory bulbectomized rat as a model of depression. Neurosci. Biobehav. Rev. 29, 627–647
Social Defeat Stress	Immobility, escape, crouching, or defensive upright stance.	5 min	Mice	Neuroendocrine disturbances and show defensive nature to the fear.	Increased threat by voice or posture Unprovoked attack and biting	It is itself a modification of chronic mild stress test in mice.	Miczek KA, O'Donnell JM. Intruder-evoked aggression in isolated and non-isolated mice: effects of psychomotor stimulants and L-dopa. Psychopharmacology (Berl). 1978; 57:47-55.
Choric Mild Stress	Weight changes, sleep disturbances, psychomotor agitation or retardation, fatigue, feelings of worthlessness or guilt.	5-10 min	Mice	Changes in social behaviour,Diminished ability to think or concentrate.	Behavioural despair, Neuroendocrine disturbances, Social interaction/avoidance Sociability	Social defeat stress	Mineur YS, Belzung C, Crusio WE. Effects of unpredictable chronic mild stress on anxiety and depression-like behavior in mice. Behav Brain Res. 2006; 175:43-50.
Fear Potential Startle	Behavioural, physiological, genetic, inversely, in subjects with alteration of learning and memory abilities, prior presentation of the light cue does not change the startle response.	10 min	Rodents	Psychomotor retardation or agitation, Fatigue or loss of energy	Decreased interest or loss of pleasure,Behavioural despair	Startle Eye-blink Modification	Kim JJ, Jung MW. Neural circuits and mechanisms involved in Pavlovian fear conditioning: a critical review. NeurosciBiobehav

							Rev. 2006; 30:188-202.
Electric Foot Shock Induced Stress	escape latency time (ELT), an index of learning,time spent in target quadrant	5 min	Mice				Herrmann L, Ionescu IA, Henes K, Golub Y, Wang NX, Buell DR, et al. Long-lasting hippocampal synaptic protein loss in a mouse model of posttraumatic stress disorder. PLoS One. 2012; 7:e42603.

MODELS ONLY USED FOR ANXIETY

ELEVATED T MAZE

The elevated T maze (ETM) was originally proposed by Graeff et al [86]. It is based on the EPM and consists of three arms: one enclosed by a lateral wall standing perpendicular to two opposite open arms of equal dimension. The whole apparatus is elevated from the floor. This model allows measurement of two different behaviours in the same animal: the conditioned response represented by inhibitory avoidance of the open arms and the unconditioned response represented by escape behavior when the animal is placed in the extremity of these arms. These responses have been related to generalized anxiety and panic disorders, respectively. The ETM was developed in response to the inconsistencies found in other animal models of anxiety, particularly the EPM, regarding drugs that interfere directly with serotonergic neurotransmission. On the day before the test, animals are exposed to one of the open arms of the T-maze for 30 min. This prior forced exposure to one of the open arms of the maze decreases the latency to leave this arm on a later trial. This result has been attributed to the habituation of behavioural reactions to novelty, which may interfere with one-way escape [87]. Twenty-four hours after pre-exposure to the open arm, the animals are tested in the ETM to measure inhibitory avoidance acquisition. To this end, each animal is placed at the distal end of the enclosed arm of the ETM facing the intersection of the arms. The time taken by the rat to leave this arm with all four paws is recorded (baseline latency). The same measurement is repeated in two subsequent trials (avoidance 1 and 2) at 30-s intervals. Following avoidance training (30 s), each rat is placed at the end of the same previously experienced open arm and the latency to leave this arm with all four paws is recorded for three consecutive trials (escape 1, 2 and 3) with 30-s intertrial intervals. A cut-off time of 300 s is usually established for the avoidance and escape latencies.

THE ELEVATED ZERO MAZE

The elevated zero maze (EZM) is a modification of the EPM that incorporates both traditional and novel ethological measures for the analysis of drug effects while eliminating the ambiguous interpretation of animal location in the centre area of the EPM [88]. The EZM is a circular runway elevated from the floor that alternates open, brightly lit areas with enclosed, dark paths. It is proposed

that the uninterrupted nature of the open versus enclosed segments of the circular arena alleviates the problems concerning the centre zone of the EPM. Similar to the behavioural measures scored in the EPM, the percent of time spent and the percentage of entries in the open areas of the EZM during the 5-min session are related to anxiety index. In this model, diazepam and chlordiazepoxide significantly increase the percentage of time spent in the open quadrants, as well as other ethological measures, such as frequency of head dips and reduced frequency of stretched attend postures in the enclosed towards the open quadrants [88]. To minimize environmental variables introduced by the presence of the investigator that may impact anxiety-like behaviours, videotaping of the session is also recommended.

SOCIAL INTERACTION TEST

The social interaction test, developed by File & Hyde, [45] was the first model of anxiety-like behavior based on ethologically relevant concepts. This test differs from the others because it involves the important component of eliminating the need to introduce aversive or appetitive conditions. In addition, it does not require previous animal training. Pairs of rodents (rats or mice) are allowed to freely interact in an arena while the time spent on social interaction is recorded. This interaction time for each of the rodents in the pair is directly impacted by the behavior of the partner animal, the pair counts as one unit for data collection purposes. If the experimental design involves one rat receiving treatment while the other serves as a control, interaction time initiated by the former is used as the dependent measure. Anxiolytic-like behavior is inferred by an increase in social interaction time while general motor activity remains unaffected. Conversely, decreased time spent engaging in social behavior would indicate anxiogenic-like behavior.

CAT EXPOSURE TEST

Defensive behaviors are observed in all mammalian species and occur in response to threatening cues, such as the presence of live predators and environmental hazards [89]. Therefore, exposure to an ethological stimulus evokes defensive responses that resemble emotional states related to fear and anxiety [90, 91]. Accordingly, predator exposure constitutes an important animal model for identification of the impact of threatening situations on different brain regions and the relationship between defensive behavior and fear-related disorders, such as panic attacks and PTSD [93, 92]. In rats, exposure to a live cat or to its odour elicits specific behaviours, such as fight, freezing, risk-assessment, and autonomic activation. These responses are accompanied by a reduction in locomotors activity and in non-defensive behaviours, such as grooming and reproduction [90, 96, 95]. Although both stimuli elicit defensive responses, exposure to a live cat induces more robust responses than exposure to its odour, accompanied by freezing and ultrasonic vocalizations. Furthermore, live cat exposure is usually resistant to habituation, has a strong contextual conditioning component, and induces anxiogenic-like effects in animals that are subsequently exposed to other anxiety models,

such as the EPM [92, 97,98]. This model was pharmacologically validated with the observation that chronic administration of panicolytic drugs decreases the fight reactions induced by the presence of the predator, whereas benzodiazepines preferentially inhibit the avoidance behaviour [100, 99]. These latter effects were also described in cat odour models, as pre-treatment with chlordiazepoxide reduced the subsequent anxiogenic-like behavior observed in the EPM and light-dark box. However, acute treatment with benzodiazepines did not reduce the defensive behaviors elicited by odour itself [101]. On the other hand, other studies showed that this treatment is able to reduce risk assessment behaviors and increase approach to the odour [94,102].

NEONATAL ISOLATION STRESS

Early-life stressful experiences, such as maternal separation or neonatal isolation, promote long-lasting neural and behavioural effects and have profound consequences on subsequent quality of life [103]. During the neonatal separation procedure, on the 2nd day after birth, the litter of the inbred strain is removed from the cage and placed in another cage for 1 hour (9 a.m. /12 a.m.) in a room located apart from the animal facility. White noise is played in the background to mask the vocalizations of other pups. After the 1-hour period, the litters are placed back with their dams in their home cages [104, 105]. The separation procedure is repeated for 8 days. This model has been used extensively to demonstrate the effect of early lifetime stress on vulnerability to addiction and in the generation of anxiety-like behaviors, which are usually observed in the adult rodents subjected to the contextual fear conditioning, EPM, or social interaction tests [106-109].

STRESS INDUCED BY CIRCADIAN RHYTHM CHANGES

Alterations in circadian rhythm have a profound impact on the physical and psychological homeostasis of an individual [111]. Rodents subjected to unexpected changes in the day-night light cycle exhibit acute stress responses [112]. Circadian rhythms are controlled by the pineal gland via melatonin secretion [112]. The stress procedure consists of lighting the home cage of the rodents during the dark phase of the cycle (e.g., lights on from 7 p.m. to 7 a.m.) and leaving it unlit in the light phase (lights off from 7 a.m. to 7 p.m.). Another possibility is to promote four or five cycles of dark-light phases (60-180 minutes) during the circadian cycle. This is a good method for induction of short-term stress responses, but repeated exposure may lead to adaptation. Responses to this stressor can be evaluated by measuring biochemical parameters associated with stress response and using the previously described animal models of anxiety [113-115].

STRESS INDUCED BY NOISY STIMULUS

Humans are constantly exposed to potentially hazardous levels of noise in modern daily life. In model animals, noise stress can be induced by using loudspeakers (15 W) connected to a white noise generator (0-26 kHz) located 30 cm above the cage. The noise can be set at a certain level (e.g., 100 dB or higher) and the animals can be exposed to the noise protocol either acutely or repeatedly (4

hours/day/15 days) [118,117]. Like those of other protocols, the behavioural effects of noise stress can be observed in animal models of anxiety and depression [119,121].

LOW TEMPERATURE INDUCED STRESS

Changes in body temperature lead to stressful responses due to activation of the thermoregulatory centre and, subsequently, of the HPA axis [121]. Abrupt reductions in temperature by using either cold water or freezer compartments have frequently been used to induce stress in laboratory animals. The most widely used protocols consist in the immersion of the animals in cold water (15-186^{o}C for 15-30 min) or placing the animals (in their home cages) in a cold, isolated environment (46C for 15-30 min). This procedure can be used in acute or chronic protocols (7-14 days) [122].

RESTRAINT & IMMOBILIZATION STRESS

Restraint stress and immobilization protocols are one of the most commonly employed procedures to induce stress-related behavioural, biochemical and physiological changes in laboratory animals [122]. Restraint stress is generally induced by keeping the animals in a cylindrical or semi-cylindrical tube with ventilation holes for 120-180 min [123,124]. In an immobilization stress protocol, animals are restrained by gentle wrapping of their upper and lower limbs with adhesive tape for 120 min [125,126]. Head movement is restricted by a metal loop wound around the neck. The procedure can be used to induce either acute or chronic stress (7-21 days). Immobilization models produce an inescapable physical and mental stress with a low rate of adaptation [128]. After restraint or immobilization stress, animals exhibit higher levels of anxiety in the EPM and other tests of anxiety [123,124].

TABULAR FORM OF ANXIETY MODEL WHICH NOT USED AS COMMON MODEL

NAME OF THE MODEL	ACTIVITY	OBSERVATION PARAMETER	TIME DURATION	ANIMAL USED	MODIFI-CATION	REFERENCE
ELEVATED T MAZE	Generalized anxiety; learning and memory features.	Open arm and the latency to leave this arm with all four paws is recorded	One day before the test: 30 minute; during test 30 min.	Rodent	Multiple elevated T-maze, y maze.	Vianamb, Tomaz c, Graefffg. The elevated T-maze: a new animal model of anxiety and memory. Pharmacology biochemist behav. 1994; 49:549-54.
THE ELEVATED ZERO MAZE	Anxiety-like behaviours, exploration	Percentage of time spent in the open sections and percentage of entries into in the open sections.	5-min	Rodent	No modification as it is itself a modification of elevated plus maze model.	Shepherd jk, Grewalss, fletcher a, bill dj, Dourish ct. Behavioural and pharmacological characterisation of the elevated ‘‘zero-maze’’ as an animal model of anxiety. Psychopharmacology (Berl). 1994; 116:56-64.
SOCIAL INTERACTION	Anxiety-like behaviour based	Freely interact in an arena while the time spent on social	Usually 5 to 15 min	Rodent	Closed box social	File SE, Hyde JR. Can social interaction be

TEST	on ethologically relevant concepts, aversive or appetitive conditions.	interaction is recorded			interaction test, open field social interaction test	used to measure anxiety? Br J Pharmacology. 1978; 62:19-24.
CAT EXPOSURE TEST	Emotional states related to fear and anxiety, Defensive behaviors	Fight, freezing, risk-assessment, and autonomic activation	5 to 10 min	Mice	Exposure in Pregnancy and lactation condition	Blanchard RJ, Blanchard DC, Rodgers J, Weiss SM. The characterization and modelling of antipredator defensive behavior. NeurosciBiobehav Rev. 1990; 14:463-72.
NEONATAL ISOLATION STRESS	Contextual fear conditioning	The effect of early lifetime stress on vulnerability to addiction	On the 2nd day after birth	All experimental animals	Memory impairments and hippocampal modifications	Kostenta, kehoe p. Neonatal isolation is a relevant model for studying the contributions of early life stress to vulnerability to drug abuse: response to marmendaletal. (2004).Devpsychobiol. 2005; 47:108-10.
STRESS INDUCED BY CIRCADIAN RHYTHM CHANGES	Physical and psychological homeostasis	Biochemical parameters associated with stress response	1 hour	Rats	Temperature rhythm changes	Nicholson s, linjh, Mahmoud s, campbell e, Gillham b, jones m. Diurnal variations in responsiveness of the hypothalamus pituitary-adrenocortical axis of the rat. Neuroendocrinology 1985; 40:217- 24.
STRESS INDUCED BY NOISY STIMULUS	Behavioural and physiological consequences by potential conservation implications	Acoustic breeding displays, mate attraction, territory defense and predator detection was observed.	5 minute to 12 hour	All experimental animals	Acetylcholine-induced bronchoconstriction modified	File SE, Fernandes C. Noise stress and the development of benzodiazepine dependence in the rat. Anxiety. 1994;1:8-12
LOW TEMPERATURE INDUCED STRESS	Activation of the thermoregulatory centre	Exposure to the olfactory And visual stimuli, rats cage-switched time.	In cold water (15-18^{o}c for 15-30 min); a cold (4-6^{o} c for 15-30 min) OR 7 days continuous exposure.	Rodents and rabbit.	Low-temperature with high-salt stress.	Jaggi as, bhatia n, kumar n, singh n, anand p, dhawan r. A review on animal models for screening potential anti-stress agents. Neurol sci. 2011; 32:993-1005.
RESTRAINT & IMMOBILIZATION STRESS	Induce stress-related behavioural, biochemical and physiological changes	cardiovascular regulation	5 to 30 min	Mice	Low stress handling and behavior modification	Campos ac, ferreirafr, guimara˜esfs, lemosji. Facilitation of endocannabinoid effects in the ventral hippocampus modulates anxiety-like behaviors. Neuroscience. 2010; 167:238-46.

MODELS ONLY USED FOR DEPRESSION

FORCED SWIMMING TEST

One of the tests most commonly used by researchers to investigate new antidepressant drugs is the FST, first described by Porsolt et al [127]. This test was developed as an animal model of depression that aimed to measure the effects of antidepressant compounds in mice. In this test, the animal is placed in a water-filled cylinder which it is unable to exit. Initially, the animal will try to escape, but eventually it adopts a posture of immobility, a passive behavior characterized by the absence of movements except for those necessary for the animal's snout to remain above the water level. The test for rats consists of two swimming exposures. The first exposure is for 15 minutes and the second is performed 24 hours after the first, with an exposure period of 5 minutes. The test for mice consists of a single 6-minute exposure, with the first 2 minutes serving as a habituation period and the last 4 minutes consisting of the test itself, which yields the duration of immobility. FST is easy to use, has very good reproducibility and is used for the selection of new antidepressant drugs. Various classes of antidepressants reduce immobility time during the FST by increasing the swimming and/or climbing time. With respect to anti-immobility, it is known that drugs affecting noradrenergic neurotransmission (e.g., imipramine) increase climbing behavior, whereas drugs affecting serotonergic neurotransmission (e.g., fluoxetine, sertraline, paroxetine, citalopram) increase swimming time [128]. The swimming time is measured by the horizontal and vertical movements of the animals as they try to scale the cylinder walls with their paws. The effects of antidepressants on FST behavior are relatively specific, since they do not increase spontaneous motor activity, unlike psych stimulants such as amphetamine and cocaine [129]. Besides the effects of antidepressant drugs, the FST can also be used to evaluate the type of depressive behavior; for example, it has been demonstrated that animals subjected to a protocol of maternal deprivation exhibit increased immobility time in the FST [130].

LEARNED HELPLESSNESS TEST

Certain types of human depression are precipitated by stressful life events, and vulnerable individuals experiencing these stressors may develop clinical depression. In this aspect, stress can be used to induce depression-like symptoms in rodent animals. One of the well-validated animal models is learned helplessness, in which a depressive-like state is induced by uncontrollable and unpredictable electrical foot-shock stress [131]. Following an uncontrollable and inescapable stress, such as exposure to unavoidable electric shocks, the animals develop a state of ‘‘helplessness’’ such that when re-exposed to the same shocks, now with an easy escape route, the animals will either display an increased escape latency or completely fail to escape [131]. Following one or more sessions of inescapable shock, rats have been shown to develop persistent changes including weight loss, alterations in sleep patterns and HPA axis activity, and a loss of spine synapses in the hippocampal

regions [132]. Reduced weight, increased motor activity, reduced libido, cognitive deficits, and changes in sleep have been observed in helpless animals. In most cases, use of the behavioural model of learned helplessness causes animals to present depressive-like behavior, as is observed clinically in human patients [133].Therefore; this model presents good face validity. In fact, animals subjected to this model respond to tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors, and electroconvulsive therapy [134]. Response to these antidepressant drugs was observed between 2-3 days after initiation of treatment. Neurobiological changes have also been observed after induction of learned helplessness. Depletion of norepinephrine and serotonin, as well as changes in the NEb norepinephrine and 5-HT1B serotonin receptors in the hippocampus, was reported. However, chronic administration of antidepressants reversed the changes in the NEb and 5-HT1B receptors. In addition, the HPA axis appears to play an important role in this animal model. Indeed, an increase in the vulnerability to learned helplessness has been observed in animals after antagonism of the glucocorticoid receptors. Furthermore, high levels of glucocorticoids and homo-cysteine – which are found in human patients with depression – have been reported in rats in an animal model of learned helplessness [135]. One advantage of learned helplessness as a model is that its symptoms are parallel to those of major depression, and most can be reversed by multiple acute (sub chronic) treatment with antidepressants (typically for 3-5 days) [134]. In addition, the cognitive (e.g., learning) and other behavioural outcomes (e.g., neurovegetative abnormalities) seem to be correlated, thus enhancing our understanding of depressive symptoms in humans. The excellent face and predictive validities of learned helplessness make it an interesting model for exploration of the pathophysiology of depression [136]. Furthermore, the model can also be generally used to measure the escape performance of mice with different mutations, showing which target genes for depression may affect vulnerability to development of a depressive-like state. However, the major drawback of this model is that most of its depression-like symptoms do not long enough following cessation of the uncontrollable shock stimulus [134]. In addition; different protocols are used in different laboratories.

CHANGING PHOTOPERIOD

More recently, it was proposed that manipulation of the light/dark cycle could characterize a new animal model of depression [146]. In this model, nocturnally active mice areexposed to long periods of artificial light (22 hours per day) for a period of 2 weeks. Exploring the interactions between these mechanisms and mood changes in diurnal animals may provide new insight into depression. Recent studies demonstrate that diurnal Fat sand rats and Nile grass rats show depression-like behavior when maintained under short-photoperiod (SP) conditions compared with animals maintained under neutral photoperiod (NP) conditions. Moreover, these behaviors were ameliorated bytreatment with bright light [145]. These animals also developed anhedoniabehavior and increased motor activity. Consistent with these behavioural changes, increased levels of corticosterone and a decrease in BDNF levels in

the hippocampus were also found, thus demonstrating face and construct validity. However, the predictive validity of this model should be examined; as treatment with the antidepressant imipramine was only able to prevent some of these behavioural and physiological changes [146]. Diurnal mice develop depressive-type behavior when subjected to experimental conditions with a decreasing photoperiod. Treatment with the antidepressants bupropion and imipramine reversed depressive behavior in these animals as shown by the FST, but not anhedoniabehavior. Other studies using the dark phase of a 12:12 light/dark cycle showed that rats exhibited depressive-like behavior. On the other hand, brief or long exposures to light treatment have an antidepressant effect on the FST [147, 148]. Taken together, these studies reveal a relation-ship between light control and depression.

SLEEP DEPRIVATION

Sleep has important homeostatic functions, and sleep deprivation is a stressor that has consequences for the brain as well as for many body systems. Although sleep deprivation is not yet a well-established model of depression, many studies show that it alters important pathways related to stress. Increased levels of messenger RNA for interleukin-1b (a pro-inflammatory cytokine) and for cortisol have been shown in rodents after sleep deprivation. The procedure of this study consisted of handling the animals gently to prevent them from sleeping. Furthermore, 72 hours of sleep deprivation in mice was induced using the platform method, which is accomplished by placing the animal on a platform submerged in water so that, when the animal falls asleep, it falls into the water and must then climb back onto the platform, thus forcing it to stay awake. This study showed that after 72 hours of sleep deprivation, there was an increase of oxidative stress in the hippocampus. A decrease in cell proliferation has also been observed after 96 hours of sleep deprivation. Some classical tests used to assess cognitive parameters in animals, such as the inhibitory avoidance and water maze tests, show deficits in learning and memory of rodents subjected to sleep deprivation, as well as aggressive behaviour andhyperactivity [137]. Even though many studies using mice have shown depressive-like behavior after sleep deprivation, it is important to note that studies in patients with depression have shown effects of antidepressants on selective slow- wave sleep deprivation [138,139]. The underlying mechanismsare still unknown, however [142], and may be related to the fact that the beneficial effects of sleep deprivation on depressive-like behaviours require an astrocyte-dependent signalling pathway. Some neurotransmitters, such as dopamine and serotonin, are altered following sleep deprivation, and these alterations are associated with behavioural changes. Sleep deprivation for short or long periods also altered gene expression of several transcription factors and genes that encode neurotransmitters and proteins involved in metabolic processes and cellular plasticity [141]. Anhedoniabehavior has been shown in rats subjected to paradoxical sleep deprivation [142]. Although the sleep deprivation protocol still has its limitations as an animal model of depression, it meets some of the criteria for a valid animal model, such as good face and constructs validity.

EARLY LIFE STRESS

Early postnatal handling and most of the all maternal separation [154], Traumatic life events in childhood have been shown to result in an increased sensitivity to the effects of stress later in life and alter the individual's vulnerability to stress-related psychiatric disorders such as depression [155].Early life stress in mice produces neuroendocrine and behavioural changes that persist into adulthood, some of which can be reverted by antidepressants [156]. The most widely used model is the maternal separation paradigm of early life deprivation, in which pups are separated from the dam for 1-24 h per day during the first two postnatal weeks. This results in increased anxiety-like and despair-based behaviour as well as increased HPA axis response, all of which can be observed in adulthood [157]. It is important to mention that shorter periods of separation tend to produce opposite effects. Thus early life challenges may conversely induce changes that prepare an individual for life in a more hostile environment and therefore be predominantly beneficial. Hence, it has be proposed that adult diseases such as depression might not be promoted by early life adversity per se, but by a mismatch of the programmed and the later actual environment in combination with a more vulnerable or resilient genetic predisposition. Although the exact physiological nature of the effects of postnatal maternal separation is not fully understood, the paradigm demonstrated its value for studying the neurobiological basis of the impact of early life stress on emotional behaviour. More recently, a new early life stress model based on similar principles has been developed. The main difference is that the new model omits the separation from the mother and thereby avoids metabolic disturbances, exhaustion, or hypothermia of the pups. This isevoked by means of fragmented maternal care, generated by reducing the amount of nesting and bedding material available to the dam [158].

TAIL SUSPENSION TEST

The tail suspension testhas become one of the most widely used models for assessing antidepressant-like activity in mice. The test is based on the fact that animals subjected to the short- term, inescapable stress of being suspended by their tail will develop an immobile posture. The FST is similar to the TST, but differs in that it can be used on both rats and in mice, whereas the TST can only be undertaken on mice. In the TST, the tails of the mice are attached and suspended by an adhesive tape. The time spent immobile by the animal during a period of 6 minutes is interpreted as a measure of depressive-like behavior. Various antidepressant medications reverse this immobility and promote the occurrence of escape-related behavior. Importantly, both the TST and FST are considered predictive models of antidepressant activity, not animal models of depression. Accordingly, they lack face and construct validity [143].

TABULAR FORM OF OTHER DEPRESSION MODEL WHICH NOT USED AS COMMON MODEL

NAME OF THE MODEL	ACTIVITY	OBSERVATION PARAMETER	TIME DURATION	ANIMAL USED	MODIFI-CATION	REFERENCE
FORCED SWIMMING TEST	Behavioural despair	Immobility latency (until first floating) Immobility duration in the water tank Swimming average speed and distance	6 min	Rodents	Porsolt Forced Swimming test,	Porsolt RD, Le Pichon M, Jalfre M. Depression: Nature. 1977; 266:730-2.
LEARNED HELP-LESSNESS TEST	Behavioural despair	Diminished ability to think or concentrate, Deficits in working and spatial memory.	5 min	Rodents	anticipatory-avoidance learning	Seligman ME, Beagley G. Learned helplessness in the rat. J Comp Physiol Psychol. 1975; 88:534-41.
CHANGING PHOTO PERIOD	provide new insight into depression	anhedonia behaviour	2 week	Rats	Controlling Photoperiod test	Becker A, Bilkei-Gorzo A, Michel K, Zimmer A. Exposure of mice to long-light: a new animal model to study depression. EurNeuropsychophar macol. 2010;20:802-12.
SLEEP DEPRIVATION	Insomnia or hypersomnia	Abnormal sleep architecture	2 week	Rats	--------	McEwen BS. Sleep deprivation as a neurobiology and physiologic stressor: all stasis and allosteric load. Metabolism. 2006; 55:S20-3.
EARLY LIFE STRESS	neuroendocrine and behavioural changes	maternal separation paradigm of early life deprivation and neurobiological basis of the impact of early life stress on emotional behaviour	2 week	Rodents	Trier social stress test	Graham YP, Heim C, Goodman SH, Miller AH, Nemeroff CB (1999) The effects of neonatal stress on brain development: implications for psychopathology. DevPsychopathol 11:545-565.
TAIL SUSPENSION TEST	Behavioural despair	Immobility latency Immobility duration "Tail-climbing"	5 min	Rodents	Tail Suspension Test - Reinvented	Cryan JF, Mombereau C, Vassout A. The tail suspension test as a model for assessing antidepressant activity: NeurosciBiobehav Rev. 2005; 29:571-625

DISSCUSION AND CONCLUSION

The animal models play an important role in the study of many pathological conditions for the human welfare.The use of common model for anxiety and depression depend upon the many reasons which include the physical condition treatment and the other symptoms, time to time many animal models are introduced which are included for the anxiety and for the depression commonly but the rarely seen the less models are separately used the models helps us a lot to understand the physiological condition of animal during the exposure or the interaction of the animal with the model.

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