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Review Article

Various models for screening of memory enhancing drugs

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ABSTRACT

Memory is the ability of an individual to record sensory stimuli, events, information etc., retain them for short or long periods of time and recall the same later when needed. Learning and memory impairment is the deficits in the memory conditions. The ability to find objects, recall previous locations and navigate throughout the world is dependent upon spatial learning and memory. Cognitive deficits have long been recognized as severe and consistent neurological disorders associated with numerous psychiatric and neurodegenerative states. Experimental models are used to study pathophysiological factors involved in learning and memory. This study explains the most useful models for the evaluation of memory impairment.

Keywords: ***Alzhiemer*** disease, Learning, Memory, Behaviour

INTRODUCTION

Memory is the most important function of the brain.[1-2]. Memory loss, also referred to as amnesia, dementia or memory impairment, is an abnormal degree of forgetfulness and/or inability to recall past events. Memory deficits have long been recognized as severe and consistent neurological disorders associated with numerous psychiatric and neurodegenerative diseases, such as Alzheimer's disease, Senile dementia, Parkinson's disease, Huntington's disease, Trauma, Chronic insomnia, Epileptic disorder and Attention deficit disorders etc. [3] However, the most common cause of memory loss has been found to be *Alzheimer's disease.* A large number of drugs are in use for the treatment of this disease and new research is going on. Although drug discovery is based upon many factors, animal models provide a crucial part in identifying chemical compounds with potential for clinical efficacy. Behavioral models for studying drugs or conditions that affect cognitive process rely on the introduction of stimulus to induce an aversive state within the organism.

MODELS FOR SCREENING OF MEMORY ENHANCING DRUGS

Based on the aversive stimuli, behavioral models for studying the neurobiology of learning and memory can be broadly classified into two main types:

a.)EXTEROCEPTIVE BEHAVIORAL MODELS
b.)INTEROCEPTIVE BEHAVIORAL MODELS

Exteroceptive Behavioral Models: Exteroceptive behavioral models are those models which pertain to stimuli that originate from outside the body or to the sensory receptors that they activate. The various Exteroceptive behavioral models are as under:

INHIBITORY (PASSIVE) AVOIDANCE [4]

One of the most common animal tests in memory research is the inhibition to imitate activities or learned habits. The term ―passive avoidance is usually employed to describe experiments in which the animal learns to avoid a noxious event by suppressing a particular behavior.

STEP-DOWN [5]

***Principle*:** An animal (mouse or rat) in an open field spends most of the time close to the walls and in the corners. When placed on an elevated platform in the center of a rectangular compartment, it steps down almost immediately to the floor to explore the enclosure and to approach the wall.

Procedure: Mice or rats of either sex are used. A rectangular box (50 x 50 cm) with electrifiable grid floor and 35 cm fits over the block. The grid floor is connected to a shock device which delivers scrambled foot shocks. The actual experiments can

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be performed in different ways. A typical paradigm consists of three phases: Familiarization: The animal is placed on the platform, released after raising the cylinder, and the latency to descend is measured. After 10 s of exploration, it is returned to the home cage. Learning: Immediately after the animal has descended from the platform an unavoidable foot shock is applied (Foot shock: 50 Hz; 1.5 mA; 1s) and the animal is returned to the home cage. Retention Test: 24 h after the learning trial the animal is again placed on the platform and the step-down latency is measured. The test is finished when the animal steps down or remains on the platform (cut-off time: 60 s).

Evaluation: The time of descent during the learning phase and the time during the retention test is measured. A prolongation of the step-down latency is defined as learning. The variability of this method is relative high; therefore, it is necessary to test large groups of animals (minimum 10 animals per group).

STEP-THROUGH [5]

Principle: This test uses normal behavior of mice and rats. These animals avoid bright light and prefer dim illumination. When placed into a brightly illuminated space connected to a dark enclosure, they rapidly enter the dark compartment and remain there. It is widely used in testing the effects of memory active compounds.

Procedure: Mice and rats of either sex are used. The test apparatus consists of a small chamber connected to a larger dark chamber via a guillotine door. The small chamber is illuminated with a 7 W/12 V bulb. The test animals are given an acquisition trial followed by a retention trial 24 h later. In the acquisition trial the animal is placed in the illuminated compartment at a maximal distance from the guillotine door, and the latency to enter the dark compartment is measured. Animals that do not step through the door within a cut-off time: 90 s (mice) or 180 s (rats) are not used. Immediately after the animal enters the dark compartment, the door is shut automatically and an unavoidable foot shock (Footshock: 1 mA; 1 s – mice; 1.5 mA; 2 s – rat) is delivered. The animal is then quickly removed (within 10 s) from the apparatus and put back into its home cage. The test procedure is repeated with or without drug. The cut-off time on day 2 is 300 s (mice) or 600 s (rats), respectively.

Evaluation: The time to step-through during the learning phase is measured and the time during the retention test is measured. In this test a prolongation of the step-through latencies is specific to the experimental situation. An increase of the step-through latency is defined as learning.

TWO COMPARTMENT TEST [6]

Principle: A rodent in an open field tends to enter any recesses in the walls and to hide there. When placed into a large box, connected through a narrow opening with a small dark compartment, the animal rapidly finds the entrance into the small chamber, enters it and spends most of its time there. The times spent in the large and small compartments are measured. The latency of the first entrance into the dark chamber and the number of crossings from one compartment into the other can be used as auxiliary criteria.

Procedure: Mice and rats of both sex and a rectangular box with a 50 x 50 cm grid floor and 35 cm high walls are used. In the centre of one wall is a 6 x 6 cm opening connecting the large compartment to a small 15 x 15 cm box with dark walls, electrifiable grid floor and removable ceiling. The connection between the two compartments can be closed with a transparent sliding door. Illumination is provided with a 100 W bulb placed 150 cm above the centre of the large compartment.

Evaluation: The times the animal spends in the large and the small compartment are measured.

UP-HILL AVOIDANCE [5]

Principle: Many animal species exhibit a negative geotaxis, i.e. the tendency to orient and move towards the top when placed on a slanted surface. When placed on a tilted platform with head facing down-hill, rats and mice invariably turn around and move rapidly up the incline.

Procedure: Rats of both sex were used and maintained under standard conditions. The experimental apparatus is a 50 x 50 cm box with 35 cm high opaque plastic walls. The box can be inclined at different angles. The floor consists of 10 mm diameter stainless steel grid bars placed 13 mm apart. To deliver the tail-shock, a tail electrode is constructed, consisting of a wire clip connected to a constant current shock source. The animal is first fitted with the tail-electrode and then placed onto the grid with its nose facing down. During baseline trials the animal's latency to make a 180° turn and initiate the first climbing response is measured. Thereafter the animal is returned to its home cage. During the experimental trials the latencies are measured and additionally a tail-shock (1.5 or 2 mA) was administered contingent on the first climbing response after the 180° turn. Immediately after the shock the animal is placed in its home cage. Retest is performed 24 h later.

Evaluation: The latencies are measured.

TRIAL-TO-CRITERIA INHIBITORY AVOIDANCE [5]

Principle: As animals experience different sensitivity to the foot shock punishment applied in the dark area, immediately after the first trial the animal is returned to the lighted area to evaluate if the task has been acquired. A criteria is established to determine the learning of the test, usually requiring the animal to remain in the lighted area for a period of 30–60 s. In this way, all the animals have a similar degree of learning independently of the amount of trials needed to attain it.

Procedure: Mice or rats are generally used. The animals are trained in the same way as in the step-through version. They are placed in the lighted compartment and after they entered with the four paws into the dark area, the door is closed and a mild foot shock is delivered. Immediately after the shock they are placed back in the lighted area for another trial. Training would continue this way until the animal remains in the lighted area for a certain period of time (30 or 60 s), a time at which the training is considered to be acquired by all the animals. The numbers of trials to attain criteria are counted as an indication of the speed of acquisition.

Evaluation: Retention of the test is measured 24 or 48 Hs later. The animals are placed in the lighted area, the door opened and the latency to step with the four paws into the dark area is recorded. A cut-off latency of 180 or 300 s is usually imposed.

ACTIVE AVOIDANCE

Active avoidance learning is a fundamental behavioral phenomenon. As in other instrumental conditioning paradigms the animal learns to control the administration of the unconditioned stimulus by appropriate reactions to the conditioned stimulus preceding the noxious stimulus. The first stage of avoidance learning is usually escaped, whereby a reaction terminates the unconditioned stimulus.

RUNWAY AVOIDANCE [7]

***Principle*:** A straightforward avoidance situation features a fixed aversive gradient which can be traversed by the animal. The shock can be avoided when the safe area reached within the time allocated.

Procedure: Mice or rats of either sex are used and maintained under standard conditions and handled for several days before the experiment. The same box as used in the step-through model can be used in this experiment. The apparatus is uniformly illuminated by an overhead light source. A loudspeaker, mounted 50 cm above the start-box, serves for presenting the acoustic conditioned stimulus(CS). The foot shock is employed by the same source as in the step-through avoidance. The animal is allowed to explore the whole apparatus for 5 min. The guillotine door is then closed and the animal is placed into the light starting area. After 10 s the acoustic CS is applied and the door is simultaneously opened. Shock is turned on after 5 s. The CS continuous until the animal reaches the safe area. It is left there for 50–70 s before returned to the same area again. The procedure starts again. The training is continued until the animal attains the criterion of 9 avoidances in 10 consecutive trials. On the next day the procedure is repeated until the same learning criterion is reached. The time needed to reach the safe area is measured.

Evaluation: The time the animal needs to reach the safe area on both days is measured. In addition, the number of errors (not reaching the safe area) is recorded.

SHUTTLE BOX AVOIDANCE (TWO-WAY SHUTTLE BOX) [4]

***Principle*:** Compared to runway avoidance, shuttle box avoidance (two-way-shuttle-box) is a more difficult task. Since the animal is not handled between trials, the shuttle box can be easily automated.

Procedure: Rats of both sexes are used and maintained under standard conditions. The apparatus used consists of a rectangular box 50 × 15 cm with 40 cm high metal walls, and an electrifiable grid floor. The box is divided by a wall with a manually or solenoid-operated guillotine door (10 × 10 cm) into two 25 × 15 cm compartments. Each compartment can be illuminated by a 20 W bulb mounted in the hinged Plexiglas lids. A fixed resistance shock source with an automatic switch (0.5 s on 1.5 s off) is used. Simple programming equipment provides for automatic delivery of the conditioned stimulus (CS) and the unconditioned stimulus (US). The apparatus is placed in a dimly light room with a masking noise background (white noise) of 60 dB. The animal is allowed to explore the apparatus for 5 min with the connecting door open and the compartment lights switched off. The guillotine door is then closed. After 20 s the light is switched on in the compartment containing the animal, and the door is opened. A tone (CS) is presented and 5 s later the floor shock is applied in the illuminated compartment and continued until the animal escapes to the dark side of the compartment, the connecting door is closed and the shock discontinued. After a variable inter trial interval (30–90 s) the light is switched on in the previous dark compartment, the door is opened and the animal is required to cross to the other side. The training is continued until the animal reaches the criterion of 9 avoidances in 10 consecutive trials. Retention is tested at different intervals after the original training by retraining the animal to the same criterion again.

Evaluation: The time the animal needs to reach the safe area on both days is measured. In addition, the number of errors (not reaching the safe area) is recorded.

JUMPING AVOIDANCE (ONE-WAY SHUTTLE BOX) [6]

Principle: Since a high degree of automation and minimum handling are additional requirements for this model, the obvious solution is a simplified one-way avoidance, allowing for the spontaneous or forced return of the animal to the start. In order to enhance the start-goal distinction a vertical gradient is introduced which requires the animal to perform a discrete response of an all-or-none character, such as the jump, which clearly differs from the more continuous translational movements required in the usual avoidance tasks.

Procedure: Rats of both sex are used and maintained under standard conditions. The apparatus used consists of a rectangular box 40 × 25 cm with 40 cm high metal walls, an electrifiable grid floor and a Plexiglas ceiling. A 12 × 12 × 25 cm opaque plastic pedestrial, mounted onto one of the narrow walls of the box provides the isolated goal area. Flush with the horizontal surface of the pedestal moves a vertical barrier, which can either be retracted to the rear wall of the apparatus to expose the goal area or pushed forward to block access to the goal completely. The animal is placed into the apparatus for 5 min with the goal area exposed (barrier re-tracted). The barrier is then moved forwards and the goal is blocked for 2 s. The first trial starts by exposing the goal area and applying an acoustic CS (1 000 Hz, 85 dB). Electric shocks – US (1.0 mA; 50 Hz; 0.5 s) – are applied 5 s later (once per 2 s), and continued together with the CS until the animal jumps onto the platform. After 30 s the barrier pushes the animal off the platform onto the grid floor. The sequence is repeated until the criterion of 10 consecutive avoidances is reached. Retention is tested on the next day until the animal reaches criterion.

Evaluation: The time the animal needs to reach the safe area on both days is measured. In addition, the number of errors is recorded.

DISCRIMINATION LEARNING [4-5]

In the experiments described above the animals have no choice between the conditioned stimuli. They have only one conditioned stimulus. The following examples illustrate the special techniques employed for discrimination among different stimulus modalities. The experiments can be classified either as simultaneous or successive discrimination paradigms.

SPATIAL HABITUATION LEARNING

Principle: The open-field test utilizes the natural tendency of rodents to explore novel environments in order to open up new nutrition, reproduction and lodging resources. The rate of exploratory behaviors exhibited in an unfamiliar environment is limited through the inherent necessity to avoid potential dangers. The observed behavior therefore is always a compromise between these conflicting interests and is regulated in part by the momentary physiological needs. Spatial habituation learning is defined as a decrement in reactivity to a novel environment after repeated exposure to that now familiar environment. This reduction in exploratory behaviors during re-exposures is interpreted in terms of remembering or recognition of the specific physical characteristics of the environment. The test can be used to examine short-term spatial memory and/or long-term spatial memory.

Procedure: The open-field apparatus is a rectangular chamber (rats: 60 × 60 × 40 cm, mice: 26 × 26 × 40) made of painted wood or grey PVC. A 25 W red or green light bulb is placed either directly above or beneath the maze to achieve an illumination density at the centre of approximately 0.3 lx. Masking noise is provided by a broad spectrum noise generator (60 dB). Prior to each trial, the apparatus is swept out with water containing 0.1% acetic acid. Housing room and the testing location are separated and animals are transported to the testing room 30 min before testing. The digitized image of the path taken by each animal is stored and analyzed post hoc with a semi-automated analysis system. In aged or hypoactive rodents testing is performed during the animal's dark phase of day. The rodent is placed on the center or in a corner of the open-field for 5–10 minute sessions. The animals are re-exposed to the open-field 24 and 96 h after the initial trial.

Evaluation: The exploratory behaviors' registered are: Rearing or vertical activity: the number of times an animal was standing on its hind legs with forelegs in the air or against the wall. The duration of single rearing as a measure of non-selective attention Locomotion or horizontal activity: the distance in centimeters an animal moved.

SPATIAL DISCRIMINATION

Principle: In the simplest case of discrimination learning the animal distinguishes between two symmetric stimulus response sets, the equal probability of which has been changes by differential reinforcement events. Position of the cues with respect to the animal's body defines the CS+ and CS–. Usually left-right discrimination is employed, while axial orientation of the body is ensured by the construction of the apparatus.

Procedure: Rats and mice of both sexes are used and maintained under standard conditions. The

apparatus used is usually a simple T- or Y-maze, with an electrifiable grid floor. The last 10 cm of each arm are separated from the rest of the apparatus by a swing-door which prevents the animal from seeing the food cup or the plastic sheet covering the grid in the goal area. A fixed resistance shock source is connected to an automatically operated switch. In an aversively motivated spatial discrimination learning the animal is trained to escape and/or to avoid foot shocks by always going to the right. Training starts by allowing the animal to explore the apparatus. Then the animal is placed on the start and after 5 s electric shocks (0.5 s, 50 Hz, 1.0 mA) are applied at 3 s intervals. The animals are trained to a criterion. On the following day the animal is retrained to the same criterion. After a 60 min interval the safe goal area is shifted to the other arm of the maze and the discrimination is reversed.

Evaluation: Errors are scored. An error means that the animal enters the wrong arm with all four legs. During retention the number of trials until the animal makes correct choices is counted.

SPATIAL LEARNING IN THE RADIAL ARM MAZE

Principle: Olton and co-workers have developed a spatial discrimination task for rodents that has been extensively used in learning and memory studies, and that has served as the basic task for one of the most important theories on the role of the hippocampus. The rat uses spatial information provided by the distal cues in the room to efficiently locate the baited arms. The radial arm-maze allows the study of spatial reference and working memory processes in the rat. In reference memory procedures, information is useful for many sessions/days and may usually be needed during the entire experiment. On the contrary, working memory procedures have a major temporal component as the information presented in the maze is useful for one session but not for subsequent ones; the rat has to remember the information during a delay interval. Correct choices in the radial arm-maze are rewarded by food.

Procedure: The apparatus is a wooden elevated eight-arm radial maze with the arms extending from a central platform 26 cm in diameter. Each arm is 56 cm long and 5 cm wide with 2 cm high rails along the length of the arm. The maze is well illuminated and numerous cues are present. Food pellets (reward) are placed at the end of the arms. During the test, rats are fed once a day and their body weights maintained at 85% of their free feeding weight to motivate the rat to run the maze. Animals are trained on a daily basis in the maze to collect the food pellets. The session is terminated after 8 choices and the rat has to obtain the maximum number of rewards with a minimum number of errors.

Evaluation: The number of errors is counted during the session.

VISUAL DISCRIMINATION

Principle: Vision is better than any other sensory system for the analysis of spatial relationships in the environment of the animal. From the retina to the cerebral cortex, the organization of the visual system ensures processing of visual information according to simple principles i.e. by fitting the distribution of light over the receptive surface to elementary geometrical concepts and by comparing these patterns with images stored in the memory.

Procedure: Rats and mice of both sexes are used and maintained under standard conditions. The apparatus consists of a square 10x10 cm start area separated by a Plexiglas sliding door from the choice area, which is connected by swing doors to the goal compartment. The grid floor in the starting and the choice areas is electrifiable. The stimulus can be attached to the swing doors. The patterns are black on a white background and have different forms. The apparatus is illuminated by a dim light. The animal is placed into the apparatus with all doors open and allowed to explore it. Then it is placed in the start and after 5 s released by raising the Plexiglas door. After another 5 s, electric shocks (1 mA, 50 Hz, 0.5 s, 1/3 s) are applied until the animal escapes through either of the open doors to the safe goal compartment where it is left for some seconds. As soon as this preliminary step is mastered, the stimulus cards are inserted, the negative door is locked and the grid section in front of this door is electrified. The animal is trained to a criterion. On the next day the animal is retrained to the same criterion and retention is expressed in savings. Another parameter which can be used to evaluate the savings is the cumulative number of errors until the criterion is reached.

Evaluation: The number of correct answers as well as the number of trials until the criterion is reached is counted.

SPATIAL LEARNING IN THE WATER MAZE [8]

***Principle*:** A task was developed where rats learn to swim in a water tank to find an escape platform hidden under the water. As there are no proximal cues to mark the position of the platform, the ability to locate it efficiently will depend on the use of a configuration of the cues outside the tank. Learning is reflected on the shorter latencies to escape and the decrease on the length of the path to find the platform. Although rodents can find the platform by using non-spatial strategies, the use of a spatial strategy is the most efficient way to escape

and young animals develop the spatial strategy after a small number of trials.

***Procedure*:** Different strains of rats are generally used. The apparatus is a circular water tank filled to a depth of 20 cm with 25 °C water. Four points equally distributed along the perimeter of the tank serve as starting locations. The tank is divided in four equal quadrants and a small platform (19 cm height) is located in the centre of one of the quadrants. The platform remains in the same position during the training days. The rat is released into the water and allowed 60–90 s. to find the platform. Animals usually receive 2–4 trials per day for 4–5 days until they escape onto the platform. Well trained rats escape in less than 10 s.

Evaluation: The latency to reach the escape platform is measured during the training days. A free-swim trial is generally performed after the training days where the escape platform is removed and the animal is allowed to swim for 30 s. With the help of a video system, the latency to reach the previous position of the platform, the number of annulus crossings as well as the time the rat spent in the training quadrant is measured. Well-trained rats show short latencies, a large number of annulus crossings and bias to the quadrant where the escape platform was located during the training sessions.

ELEVATED PLUS MAZE (EPM) TASK [9]

Principle: The general principle of elevated plus maze (EPM) is that more anxious the subjects are, the less likely they will be to explore an uncomfortable, risky, or threatening environment. Thus, previous stress, presence of a predator, previous handling, manipulation of stress hormones and peptides all effect behavior in the EPM.

Procedure: The elevated plus maze serves as the exteroceptive behavioral model (wherein the stimulus existed outside the body) to evaluate learning and memory in mice/rat. The apparatus consists of two open arms (16 cm × 5 cm) and two covered arms (16 cm × 5 cm × 12 cm). The arms ex-tended from a central platform (5 cm × 5 cm) and maze are elevated to a height of 25 cm from the floor. The testing session consists of putting the animal in the apparatus and recording the following behaviors: total time spend in open arm, total time spend in closed arm, total no. of grid crosses, open arm entities, closed arm entities.

Evaluation: The mouse is placed at the end of an open arm, facing away from the central platform or at the centre of the maze. Transfer latency (TL) is taken as the time taken by the mouse to move into any one of the covered arms with all its four legs. TL is recorded on the first day. If the animal does not enter into one of the covered arms within 90 sec., it is gently pushed into one of the two covered arms and the TL is assigned as 90 sec. The mouse is allowed to explore the maze for 10 sec and then re-turned to its home cage. Retention of this learned –task is examined 24 H after the first day trial.

INTEROCEPTIVE BEHAVIORAL MODELS

Interoceptive models are those models which pertain to stimuli originating from within the body that are related to the functioning of the internal organs or the receptors they activate. The interoceptive behavioral models (inducing agents for memory impairment) for evaluating memory enhancing activity mostly include chemical agents which induce impairment in the memory of subjects by acting on various receptors or interfere with different neurotransmitters. Various such chemicals and drugs used as interoceptive behavioral models are as follows:

Table 1 : Memory impairment inducing drugs along with their doses

S. NO	INDUCING AGENTS	DOSE AND REFERENCE
01	**Scopolamine Hydrobromide**	0.4 mg, 0.6 mg, 1 mg/kg b.w/i.p
02	**Diazepam**	1 mg/kg b.w/i.p
03	**Phenytoin**	5 mg, 12.5 mg, 25 mg, 50 mg, 75 mg/kg b.w/i.p
04	**MK-801**	0.15 mg/kg b.w/i.p
05	**Streptozotocin**	3 mg/kg b.w/i.p
06	**7-Nitroindazole(7-NI)**	5 mg, 10 mg, 20 mg, 50 mg/kg b.w/i.p
07	**Phosphamidon**	1.74mg/kg b.w/p.o
08	**Triazolam**	0.5 mg/kg b.w/i.p
09	**Zolpidem**	20 mg/kg b.w/i.p
10	**Alcohol**	0.5 g, 2 g/kg b.w/p.o
11	**Midazolam**	2 mg/kg b.w/i.p
12	**D-galactose**	50 mg/kg b.w/i.p
13	**Sodium Nitrite ($NaNO_2$)**	0.5-10 mg/kg b.w,s.c
14	**β-Amyloid peptide**	10µg in 10µl i.c.v/animal

Out of the above models, administration of Scopolamine Hydrobromide has been shown to produce a marked impairment of memory in rats as well in human beings [10-21].

SCOPOLAMINE INDUCED MEMORY IMPAIRMENT:

Scopolamine, also known as levo-duboisine and hyoscine, is a tropane alkaloid drug with muscarinic antagonist effects. It is among the secondary metabolites of plants (family-Solanaceae) [22]. It can be administered orally, subcutaneously, opthalmically and intravenously, as well as via a transdermal patch [23]**.** Scopolamine has been used in the past to treat addiction to drugs such as heroin and cocaine [24]. It also causes memory impairments to a similar degree as diazepam [25].

***Principle and Mechanism of Action*:** The administration of the anti-muscarinic agent scopolamine to young human volunteers produces transient memory deficits [26]. It has been shown to impair memory retention when given to mice shortly before training in a dark avoidance task [27]. It is well known that cholinergic neurons and projections play important roles in the regulation of several survival functions, including learning, memory, movement and the control of cerebral blood flow in the central nervous system [28]. In addition, Acetylcholinesterase (AChE) plays an important role in cholinergic functions [29]. Scopolamine, a muscarinic cholinergic receptor antagonist, has been widely adopted to study cognitive deficits in experimental animals. After i.p. injection of scopolamine, the cholinergic neurotransmission gets blocked, leading to cholinergic dysfunction and impaired cognition in rats. It has also been reported that memory impairment induced by scopolamine in rats is associated with altered brain oxidative stress status [30] and several research findings have implicated oxidative stress in the pathophysiology of dementia among other age related neurodegenerative disorders [31]. Therefore, rats with scopolamine-induced memory deficits are used as an animal model for screening anti-dementia drugs [32]. Usually 0.4 mg/kg b.w i.p of Scopolamine Hydrobromide is used to produce memory impairment in experimental animals (rats/mice) [33-34]. However, higher doses (0.6 mg/kg; 1mg/kg) [35] have also been used to induce memory impairment in rats/mice for experimental purposes. The ability of a range of different cholinergic agonist drugs to reverse the amnesic effects of scopolamine is now well documented in animals and human volunteers. However, the neuropathology of dementia of the Alzheimer type is not confined to the cholinergic system [36].

CONCLUSION

The present review opens vista for the evaluation of learning and memory condition in various animal models. However it is challenging task to develop appropriate animal model for dementia in the absence of truly affective therapeutic agent. For an ideal animal model it should exhibit some or all the behavioral and neurological dysfunction known to be associated with disorder. In the meantime many models are developed successfully which are currently used and there is huge scope for the development of new advanced screening models for learning and memory enhancer drugs.

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