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The contribution of all maze system to Neuropharmacology and Behavioural studies - A Review

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Abstract

All maze system with video tracking software is useful to study how drugs affects cellular function in the nervous system and the way by which they influence the behaviour. This review focusses on Elevated plus maze, Y maze, T maze, Zero maze, Water maze, Multiple unit open field enclosure, Radial arm maze, Tail suspension unit, Light and dark unit, Novel object recognision test unit, Conditioned Place Preference unit and Barnes maze, which are used in the evaluation of neuropharmacological and behavioural studies.

Keywords: Neuropharmacology, Behavioural studies, All maze system, Video traking software

Introduction

Neurodegenerative and neuropsychiatric disorders are widespread, causing premature morbidity and increasing social and personal burden. These disorders are characterized by diverse cognitive impairments, which can vary significantly within diagnoses, but often have overlapping deficits between disorders. Impairments in working memory and cognitive or behavioural flexibility are commonly reported in many neurological and neuropsychiatric disorders such as Alzheimer"s disease, Parkinson"s disease, schizophrenia, depression, substance abuse and autism Impairments in working memory and cognitive flexibility have become well -defined behavioural endophenotypes and combined with animal models have become an integral part of translational research[1].

All maze video tracking software

All maze video tracking software is a software package for automated analysis of rodent behavior in laboratory settings. It tracks and analyses the behavior, movement and activity of experimental animals without the use of sensor.

Elevated plus maze

The EPM was first introduced as a simple, rapid rodent assay to identify anxiolytic pharmacological agents. The test is based on the rodent exploratory pattern, which avoids open areas and favors moving along walls (thigmotaxis). The test does not include aversive stimuli, such as shock, bright light, or loud noise, that evoke freezing, startle, or escape behaviors. The subjects are placed in the center of an elevated platform shaped as a "plus" and spontaneous behavior is recorded over the next 6–10 min. Two opposite arms are enclosed in walls and the other two are "open." The most common indices of anxiety are time in the open arms or number of entries into the open arms.[2] Elevated plus maze is available for both mice and rat.

Y maze

This test is based on the natural drive of rodents to explore novel environments and test the short-term spatial recognition memory. This test requires neither food deprivation (unlike the radial maze) nor electrical foot-shock (unlike the light/dark box), which could modify the motivational and emotional status of the animal. The Y-maze test was successfully applied to study the effect of age, administration of various drugs and food supplements, as well as various stressors, on spatial memory performances. The Y-maze can be used as a measure of short term memory, general locomotor activity and stereotypic behavior.

The Y-maze consists of three identical arms mounted in the shape of a "Y" (120°, 41cm long and 15cm high). The procedure consists of two sessions, each about 30 minutes. During the first session, 15 minutes in duration, one arm (the novel arm) is blocked but the mouse can inspect the other two open arms. During the second session, all arms are open. The position of the animal in the maze is usually recorded by a tracking system. Parameters to be analyzed are: first arm entered, number of entries into each arm, and time spent in each arm. The dependent variable is time spent in the novel arm of the Y-maze. During the second session, animal with intact spatial memory will usually make the first turn into the novel (i.e., previously blocked arm) and spend approximately 60%–70% of the time in that arm. Animal with spatial memory deficits do not exhibit a significant difference in arm entries, presumably as a consequence of impaired ability to discriminate between previously seen and novel objects.[3]Y mazes are available for both rat and mice

T-maze

T- maze challenges the rat to choose either the left or right arm to collect a reward such as food . The animal may learn to go to a specific location within the room, or to make a specific motor response at the choice point. However, if the animal approaches the choice point from the other direction in a 'probe trial,' the two behaviors will lead in opposite directions and so can be distinguished from each other. In such probe trials it is important neither to reward the animal nor violate its expectation of reward, if learning in the standard configuration is to continue unchanged. For this reason the animal might be removed from the maze after the choice point, or might be unrewarded if the experiment is run with a partial (i.e., intermittent) reinforcement schedule.[4]T mazes are available for both rat and mice.

Zero maze

The Elevated Zero Maze is used to assess anxiety, emotionality and reactivity. It is a more novel variation of the Elevated Plus Maze. Like the Plus maze, the arena is elevated and consists of two open areas and two closed areas (both of equal area). Both of these areas are equipped with rows of infrared photocells interfaced with a computer. While the open areas are, by design, anxiogenic, the animal is free to move into the closed areas. Zero mazes are available for both rat and mice.

Water maze

The water maze (WM) is often used for the evaluation of effects of various compounds on memory functions, e.g., memory formation, consolidation, and retrieval effects due to its advantages and broad utilization. The Morris WM is a widely used measurement of visuospatial learning that has been demonstrated to have high validity in identifying cognitive effects of various brain lesions and the effects of drugs used to treat cognitive deficits. Special motivation such as food and water deprivation is not required for the WM performance. The effect of odor cue is eliminated in the WM. In addition, rats are forced to swim in the WM. They cannot choose whether to move, so failure to respond is not a confounding issue. The place-learning version with submerged platform can be used for working memory tests. The WM can be used to measure spatial learning and memory in the case of the evaluation of cognitive impairment in rats because of the aforementioned advantages.

The animal perform cognitive tasks that require spatial learning and memory—the ability to acquire a cognitive representation of location in space and the ability to effectively navigate the environment in the WM. Memory alterations appear to occur mostly in secondary memory systems and are reflected in the storage of newly acquired information. It is thought that hippocampus mediates allocentric spatial navigation (i.e., place learning) and prefrontal cortex is critical in acquiring the rules that govern performance in particular tasks (i.e., procedural knowledge), whereas the dorsomedial striatum mediates egocentric spatial orientation (i.e., response and cue learning).

The WM consists of a black circular pool (180 cm diameter×80 cm high) filled to a depth of 25 cm with water at room temperature. The pool is imaginarily divided into four equal compartments numbered 1–4 (clockwise). The black antireflective circular escape platform (15-cm diameter) is placed into compartment number 1 or 4, 20 cm off the pool wall. The platform is sunk 2 cm below the water surface so it is not visible to the rats because of the water mirror effect. The yellow rectangle (30×40 cm^2) is fixed on the pool wall that is closest to the platform as the spatial conditional cue. Its place is variable according to the platform. Another dark rectangle is randomly fixed on the pool wall in different compartments (without platform) as the negative conditional cue. Around the pool there are several stable extramaze cues in the room that the rat could use to navigate the maze. However, the impact of extramaze cues is not significant because of high maze walls.[5]Water mazes are available for rat and mice.

Multiple unit open field enclosure

Ambulation is the most common behavior studied but others such as latency or rearing can also be measured. Most often, rodent behavior is analyzed in a bare maze. However, the addition of objects, either one or many to the maze floor, adds the ability to see how the subject interacts with novel additional stimuli[2]. Relevant parameters when objects are presented are typically the number of approaches to an object or in some cases, preference or aversion for one object over another.

The open field test (OFT) is a common measure of exploratory behavior and general activity in both mice and rats, where both the quality and quantity of the activity can be measured. It provides an easy and fairly rapid assessment of well-defined behaviors requiring no training to the test subject and little to no specialized training for the human administering the test. Principally, the open field (OF) is an enclosure, generally square, rectangular, or circular in shape with surrounding walls that prevent escape. The most basic and common outcome of interest is “movement”; however, this can be influenced by motor output, exploratory drive, freezing or other fear-related behavior, sickness, relative time in circadian cycle, among many other variables. Distance moved, time spent moving, rearing, and change in activity over time are among many measures that can be tabulated and reported.

The OFT is also commonly used as a mechanism to assess the sedative, toxic, or stimulant effects of compounds. Thus, the OFT measures a number of facets of behavior beyond simple locomotion. As such, the test has a number of uses and is included in almost every thorough analysis of rodent behavior. [6]

Radial arm maze

The radial arm maze consists of an array of arms, usually eight or more, which radiate from a central starting point. At the end of each arm is a cup that may or may not contain a food reward. Animals are trained to recognize that only one of the arms will contain food. Investigators measure the amount of time it takes for animals to find the arm leading to food, as well as the number of times it traverses an arm it has previously visited. Exploring a previously visited arm indicates that the animal did not remember previously choosing that spatial path. This is a relatively difficult task for rodents, requiring several days or weeks to train rats and many weeks to train mice. Unlike the Morris water maze and the Barnes maze, the radial arm maze does not use distant visual cues to aid spatial learning. [7]Radial arm mazes are available for rat and mice.

Tail suspension test unit

A novel test procedure for antidepressants was designed in which a mouse is suspended by the tail from a lever, the movements of the animal being recorded. The total duration of the test (6 min) can be divided into periods of agitation and immobility. Several psychotropic drugs were studied: amphetamine, amttriptyline, atropine, desipramine, mianserin, nomifensine and viloxazine. Antidepressant drugs decrease the duration of immobility, as do psychostimulants and atropine. If coupled with measurement of locomotor activity in different conditions, the test can separate the locomotor stimulant doses from antidepressant doses. Diazepam increases the duration of immobility.

The main advantages of this procedure are (1) the use of a simple, objective test situation, (2) the concordance of the results with the validated "behavioral despair" test from Porsolt and, (3) the sensitivity to a wide range of drug doses[8]. Tail suspension test units are available for rat/mice.

Light & dark unit

The test is based on the natural aversion of animal to brightly illuminated areas and on their spontaneous exploratory behavior in novel environments. The test is sensitive to anxiolytic drug treatment. The apparatus consists of a dark chamber and a brightly illuminated chamber. Animals are allowed to move freely between the two chambers. The number of entries into the bright chamber and the duration of time spent there are indices of bright-space anxiety in mice[9]. Light and Dark unit is available for rat and mice.

Novel object recognision test unit

Novel object recognition test (NORT) and its variants have been widely used as tools to investigate the neurobiology of memory. These studies have involved the evaluation of different memory processes, such as acquisition, consolidation (and reconsolidation) and retrieval, as well as the brain mechanisms that underlie these processes. Rodents have a natural tendency to spend more time exploring novel objects than familiar objects. In addition, they show increased exploration of familiar objects in a novel location and are able to detect the temporal order of the presentation of familiar objects. A prominent advantage of this paradigm, compared to other traditional memory tasks (operant delayed nonmatching to sample, radial arm maze, Morris water maze and avoidance tests), is that a reinforcement protocol is not necessary, i.e., there is no need of extensive training. In addition, NORT involves exploration activity in response to novelty in an open field, which is comparable to the experience of animals in their natural habitat; thus, this contributes to its high

ethological validity. The detection of novelty in the environment is essential to survival and reproductive success as animals need to recognize conspecifics in a social group, objects and cues in the surroundings and routes and places.

Some NORT evaluates separate or combined components of the memory of an object; in the former nonassociative aspects of episodic-like memory (ELM) are involved, whereas in the latter two components of ELM (associative) are simultaneously required, 'what–where' or 'what–when'. Recent variants of NORT involve the simultaneous occurrence of 'what–where–when' memory. Thus, it is likely that these different variants of NORT involve different cognitive processes, which could be subserved by different brain neural circuits[10]. Novel object recognition test unit are available for rat and mice.

Conditional place preference test unit

The conditioned place preference paradigm is a standard preclinical behavioral model used to study the rewarding and aversive effects of drugs. Although a number of different designs and apparatuses are used in this model, the basic characteristics of this task involve the association of a particular environment with drug treatment, followed by the association of a different environment with the absence of the drug (i.e., the drug's vehicle). A common variation of this design consists of a three-compartment chamber with the outer compartments being designed to have different characteristics (e.g., white vs. black walls, pine vs. corn bedding, horizontal grid vs. cross-grid flooring). The center compartment has no special characteristics and is not paired with a drug, and the gates between the compartments can be opened to allow an animal to pass freely between them. During training, an animal (typically a rat or mouse) is given an injection of a drug with potentially rewarding or aversive properties, and is then placed into one of the outer compartments for several minutes. On the following day, the rat is injected with the drug's vehicle and then placed in the opposite compartment. Generally, these daily sessions alternate between drug and vehicle for 2 or 3 days each. Afterward, a test session is conducted, which consists of placing the animal in the center compartment and then, after opening the gates to both of the outer compartments, recording the time the animal spends in each of the outer compartments during the session.

A conditioned place preference (CPP) is found if the animals spend significantly more time in the drug-paired compartment versus the vehicle-paired compartment. On the other hand, if the animals spend significantly more time in the vehicle-paired compartment versus the drug-paired compartment, then this is considered a conditioned place aversion (CPA). Typically, drugs of abuse, such as cocaine, produce CPP, and drugs that elicit aversive effects, such as lithium chloride, produce CPA. As with other behavioral models used in pharmacology research, the behavioral effects of drugs used in the CPP paradigm depend on species, strain, route of administration, time interval of drug administration, dose concentration, and the CPP apparatus used. Many drugs of abuse produce both CPP and CPA, depending on the dose administered. In drug-dependent animals, withdrawal effects generally produce CPA. Because the CPP paradigm generally provides a reliable indicator for studying the rewarding effects of drugs that require relatively little training compared to self-administration paradigm, the CPP paradigm has been commonly used in conjunction with standard neuroscience techniques to elucidate the subjective effects of drugs[11].

Barnes maze

Barnes maze examines spatial learning and memory, but its physiological basis is different. The Barnes maze consists of a circular table with holes around the circumference, placed in a room with visual cues in the periphery. Most of these holes lead to an open drop to the floor, but a single hole leads to a drop box, a dark box in which the animal can hide. A rodent is naturally motivated to avoid open spaces and bright lights,

and therefore attempts to find the drop box. In initial trials, the scientist gently leads the animal to the drop box. In subsequent trials, the animal is placed in the center of the table and must find the drop box on its own. After a few trials, rodents typically remember which hole contains the drop box and quickly proceed in a direct path toward the hole. Investigators can measure the amount of time to find the correct hole, the number of incorrect holes explored, and the length of the exploratory path. The Barnes maze is considered to be less stressful than the Morris water maze[12]. Barnes mazes are available for both rat and mice.

Conclusion

Neuropsychiatric disorders together with brain connectivity and emotion are the major areas in neuroscience. Alzheimers disease (AD), Parkinsons disease (PD) and related dementias are the most prevalent aging related neurodegenerative disorders of the central nervous system affecting more than 17 million people worldwide respectively. As a result of global trend in population aging, number of patients with AD, PD and related dementias is projected double over the next 20 years. These neuropsychiatric disorders poses significant socioeconomic burden on society. So it is the need of the hour to do research in neuro and behavioral pharmacology. All maze system with video tracking software will explore the potential of various novel compounds in neuro and behavioral pharmacology.

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