



Research report

The double-H maze test, a novel, simple, water-escape memory task: Acquisition, recall of recent and remote memory, and effects of systemic muscarinic or NMDA receptor blockade during training

Sarah Pol-Bodetto, H el ene Jeltsch-David, Lucas Lecourtier, Nathalia Rusnac, C elia Mam-Lam-Fook, Brigitte Cosquer, Karin Geiger, Jean-Christophe Cassel*

Laboratoire d'Imagerie et de Neurosciences Cognitives, FRE 3289, Universit e de Strasbourg – CNRS, IFR 37 de Neurosciences – GDR 2905 du CNRS, Facult e de Psychologie, 12 rue Goethe, F-67000 Strasbourg, France

ARTICLE INFO

Article history:

Received 15 September 2010

Received in revised form

15 November 2010

Accepted 20 November 2010

Keywords:

Automatism

Declarative-like memory

Hippocampus

Learning

Maze

Muscarinic

N-methyl-D-aspartate

Procedural memory

Rat

Spatial

Striatum

ABSTRACT

To explore spatial cognition in rodents, research uses maze tasks, which differ in complexity, number of goals and pathways, behavioural flexibility, memory duration, but also in the experimenter's control over the strategy developed to reach a goal (e.g., allocentric vs. egocentric). This study aimed at validating a novel spatial memory test: the double-H maze test. The transparent device made of an alley with two opposite arms at each extremity and two in its centre is flooded. An escape platform is submerged in one arm. For experiments 1–3, rats were released in unpredictable sequences from one of both central arms to favour an allocentric approach of the task. Experiment 1 (3 trials/day over 6 days) demonstrated classical learning curves and evidence for recent and nondegraded remote memory performance. Experiment 2 (2 days, 3 trials/day) showed a dose-dependent alteration of task acquisition/consolidation by muscarinic or NMDA receptor blockade; these drug effects vanished with sustained training (experiment 3; 4 days, 3 trials/day). Experiment 4 oriented rats towards a procedural (egocentric) approach of the task. Memory was tested in a misleading probe trial. Most rats immediately switched from response learning-based to place learning-based behaviour, but only when their initial view on environmental cues markedly differed between training and probe trials. Because this simple task enables the formation of a relatively stable memory trace, it could be particularly adapted to study consolidation processes at a system level or/and the interplay between procedural and declarative-like memory systems.

  2010 Elsevier B.V. All rights reserved.

1. Introduction

Spatial cognition, which relies upon declarative memory in humans, can be weakened in elderly (e.g. [1,2]), and is markedly altered in Alzheimer's disease (AD) patients (e.g. [3–6]). Similar alterations have been induced in laboratory rodents by lesions of selected brain regions or transmitter systems, or by the administration of drug treatments activating or blocking receptors of interest, among which cholinergic muscarinic receptors and glutamatergic NMDA receptors have awaked much interest (e.g. [7]). Spatial memory deficits have also been characterized in aged mice and rats, as well as in a variety of transgenic mice developed to reproduce one or more of the neurodegenerative features or histopathological signatures of various diseases (e.g. [8,9]), or in which essential steps of learning-triggered intracellular signaling pathways have been knocked-out (e.g. [10–12]).

To characterize spatial memory in rodents, research usually assesses the effects of experimental treatments in a variety of maze tasks (e.g. [13,14]). In these tasks, animals may achieve good performance by using strategies based on their acquired knowledge of the salient landmarks of their testing environment (a so-called "allocentric" strategy) or on bodily cues becoming central for the organization of displacements (a so-called "egocentric" strategy). These tasks can also be distinguished according to the degree of flexibility with which an animal may try to solve them. In some of them (e.g., the Stone maze), flexibility is weak: the task consists in acquiring the only correct route connecting a start point with a goal, leaving no space to alternative strategies or short cuts, reducing the spatial load on memory function in a training level-dependent manner, and facilitating the emergence of cognitive routines or motor response-based automatisms. In other tasks leaving more room to flexibility, such as Olton's radial maze [40] or the ziggurat maze [15] – formerly called the cone field task [16] – there are several goals, food (or other rewards) being provided at various locations. Good performance may be achieved by an allocentric or an egocentric strategy. In the largely used Morris water maze (e.g.

* Corresponding author. Tel.: +33 03 68 85 19 52; fax: +33 03 68 85 19 58.
E-mail address: jcassel@unistra.fr (J.-C. Cassel).

[17]), a dry version of the latter (e.g. [18]) or the Barnes maze (e.g. [19]), animals have to learn a given location to which they have to navigate. Although the item to be learned and remembered is single, the search patterns and routes to this location are virtually infinite. Even with such tasks, animals do not necessarily use an allocentric strategy. Indeed, in e.g. the water maze, rats and mice can reach the escape point by swimming in circle along the pool border at about the distance from the border at which the platform is placed: they can know how to reach the platform without knowing precisely where it is immersed [20].

The problem with the tasks in which a specific route must be learned is that animals can solve them without having to use a spatial memory. In many if not all of the others, the problem is less that animals can solve them with alternative strategies, and thus without having to form a spatial memory, than the fact that the experimenter has no or relatively poor control over which spontaneous strategy an animal is going to develop during training. In addition, the allocentric solution to these tests, which are often used to screen the effects of cognition-enhancing drug candidates in pre-clinical approaches, requires relatively complex mental processing; if one goes back to the notion of model, especially of human memory systems, it is noteworthy that not all of our daily behaviours rely upon such complex operations. Under some instances, it might be interesting to know the effects of cognition-enhancing drug candidates on relatively simple behaviours. Regarding the aforementioned drawbacks on the use of alternative strategies, on the lack of control by the experimenter of an animal's strategy and on task complexity, the recently introduced starmaze (e.g. [21,22]) appears an interesting compromise as, being a relatively simple navigation task preventing possible deviations from an ideal start-to-goal trajectory, it enables an extremely fine a posteriori analysis of an animal's spontaneous strategy during a retention test. However, as in the other tasks, the experimenter still has limited control over the strategy used by the animal to achieve good performance; for instance, mice can be forced into procedural routines, but the protocol is based on using a mobile goal, which is not very "ecological". We therefore conceived a novel test device, which we call the *double-H maze*, and in which rodents have to learn to reach the location of an escape platform submerged in water, but the pathway possibilities from the start to the goal are limited to a reasonably low number and training may be adapted such as to shape an allocentric or an egocentric strategy.

2. Materials and methods

2.1. Subjects

For the currently reported four experiments, we used a total of 219 adult, male Long-Evans rats weighing between 240 and 268 g at the start of each experiment. They were provided by the Centre d'Élevage R. Janvier, Le Genest St-Isle, France. All rats were kept in individual transparent Makrolon cages (42 cm × 26 cm × 15 cm) in temperature-controlled (23 ± 1 °C) rooms that were maintained on a 12: 12 h dark–light cycle (light on at 7:00 AM). All rats were housed with *ad libitum* access to food and water throughout the experiment. All procedures involving animals and their care were conducted in conformity with the institutional guidelines that are in compliance with the national council directive no. 87848, October 19, 1987, *Ministère de l'Agriculture et de la Forêt: (C-67-482-13)*, the French law on researcher agreement (licence 67-215 to JCC; other authors under the former's responsibility), and international (NIH publication no 85-23, revised 1985) laws and policies. All efforts were made to minimize the number of animals used with respect to statistical constraints.

2.2. The double-H maze test

Regarding the device, the principle of the test and the possible protocols, we aimed at setting up a test that, compared to all existing ones, would (i) assess spatial memory, (ii) be simple enough to be learned in a rather short period of training or, using sustained training, under conditions of moderate neuronal dysfunctions, (iii) enable a control over the strategy that an animal may develop to solve the task (i.e., maintain the animal in a strategy based on declarative-like memory vs. a procedural memory-based strategy), (iv) establish a memory that would result in a minimal

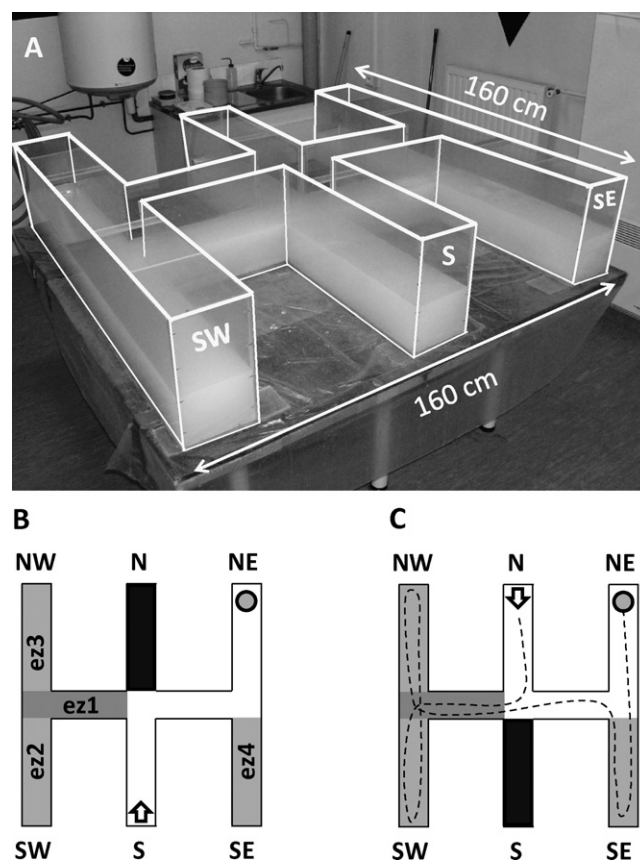


Fig. 1. The double-H maze. (A) Photograph showing the general aspect of the maze. The edges have been redrawn in white to generate a more contrasted illustration. The maze, holding in a square of 160 cm × 160 cm, has an internal surface of 10,949 cm². For the photograph, it has been filled with opaque water to about 14 cm in height. (B) Bird view drawing of the double-H maze, on which the error zones (ez1–ez4) are indicated in grayish. In this example, the error zones are defined according to a task in which the rat is released from the S arm, from where it has to swim to a platform submerged at the extremity of the NE arm (O). The arm facing the start arm has been filled in black to indicate that it is closed. To close it, we use a transparent guillotine door. (C) Same drawing as in B, but with a start from the N arm (and this time the S arm is closed) and modification of the error zones according to the new start point. The hatched line indicates a theoretical example of a rat's swim path in which 4 errors are counted (ez1, ez3, ez2 and ez4) before the platform is reached; all these errors are counted as initial errors as none of them was repeated.

performance decline over time, as usually seen in fear conditioning tasks, but more seldom in tasks assessing spatial memory in the absence of an overtraining program.

2.2.1. Apparatus

In a bird view, the general layout of the apparatus roughly corresponds to the shape of two contiguous Hs. It is made of three parallel run arms, 160 cm in length and 20 cm wide, connected to each other at the level of their centre by a perpendicular one (see Fig. 1A). Each of these arms is equipped with side walls, 35 cm high. By convention, the intermediate arm's extremities are designed as north (N) and south (S), respectively. One or alternatively both of these extremities are used as start arms in our basic training protocols (see below). The extremities of both other side arms are corresponding to our four potential target locations. They are termed north-west (NW), north-east (NE), south-west (SW) and south-east (SE) hereafter (see Fig. 1A–C). All elements of the apparatus are made of transparent Plexiglas. They have been glued and subsequently screwed to each other, and all joints are waterproofed by application of silicone joints in all internal angles. The double-H is placed on a table, 80 cm from the floor, in a large room with well-contrasted cues on the walls.

2.2.2. General behavioural procedures

The double-H is flooded with water (21 °C) to a height of 15 cm, thus with an approximate volume of 170 L. The water is rendered opaque with powdered milk (about 250 g). A platform, 11 cm in diameter, 14 cm high, ballasted by gravel, is immersed at one extremity of one of the four goal arms, 1 cm underneath the water surface. For the rat, the task consists in learning to swim from the start point – which

Download English Version:

<https://daneshyari.com/en/article/6259912>

Download Persian Version:

<https://daneshyari.com/article/6259912>

[Daneshyari.com](https://daneshyari.com)