Behavioural Brain Research 236 (2013) 102–109

Contents lists available at SciVerse ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

# Profound retrograde but absence of anterograde amnesia for cued place learning in rats with hippocampal lesions

Juan M.J. Ramos*

*Department of Psychobiology, Campus Cartuja, University of Granada, Granada 18071, Spain*

## HIGHLIGHTS

- Under certain training conditions hippocampal rats can learn spatial locations.
- A constant intramaze cue in the goal arm overcomes the deficit in place learning.
- After learning, the removal of the intramaze cue has no effect on spatial memory.
- Although spatial learning is preserved a profound deficit in retention is observed.
- Regardless of the type of training method used, hippocampal lesions produce retrograde amnesia.

## ARTICLE INFO

*Article history:*
Received 27 May 2012
Received in revised form 20 August 2012
Accepted 23 August 2012
Available online 1 September 2012

*Keywords:*
Hippocampus
Spatial cognition
Consolidation
Retention
Amnesia
Radial maze

## ABSTRACT

Previous studies in our lab have shown that slight modifications in the spatial reference memory procedure can overcome the deficit in spatial learning typically observed in rats with hippocampal damage. However, it is unknown if memory acquired under such training circumstances is spared after hippocampal lesions. With this aim a four-arm plus-shaped maze and a spatial reference memory paradigm were used, in which the goal arm was doubly marked: by an intramaze cue (a piece of sandpaper positioned on the floor of the arm) and by the extramaze constellation of stimuli around the maze. Experiment 1 replicated previous findings showing that hippocampally damaged rats can learn a place response just as well as the controls when the intramaze cue is present during the training, but they are unable to do so in the absence of the intramaze signal. When the learning procedure was doubly signaled, a transfer test performed 24 h after the end of acquisition demonstrated that lesioned rats showed perfect memory for the goal arm when the intramaze cue was removed. Experiment 2 investigated the effect of hippocampal damage 1 day after the learning. Results showed that regardless of the training procedure employed (with or without the intramaze cue), hippocampal lesions produced a profound retrograde amnesia. Thus, although the absence of anterograde amnesia suggests that structures other that the hippocampus can take charge of the acquisition, the presence of retrograde amnesia indicates the critical role of the normal hippocampus in the long-term formation of allocentric information.

© 2012 Elsevier B.V. All rights reserved.

## 1. Introduction

A considerable amount of data has led to the view that the hippocampus is an essential component of the brain system involved in allocentric memory, which depends on forming complex relationships among distal environmental cues [1]. Supporting this idea a large number of studies have demonstrated the existence of place cells within the hippocampus [2–4]. Interestingly, place cells, besides responding to incoming perceptual information, are activated by proprioceptive and vestibular signals generated by movement [5], suggesting that the hippocampus is an essential part of a path integration (or dead-reckoning) system. Thus, the path integration process complements the allocentric processing carried out by the place cells during navigation [6–8]. Additionally, lesions studies have clearly established a central role for the hippocampus in allocentric memory by demonstrating that hippocampal damage produces a profound anterograde and retrograde impairment in tasks of allocentric memory in rats and humans. However, it does not affect other types of spatial paradigms such as memory for particular landmarks and egocentrically based representations [9–19].

In recent years, however, a significant number of studies have challenged the essential role initially proposed for the hippocampus in allocentric learning and memory. Firstly, within the medial

* Correspondence address: Departmento de Psicobiología, Campus Cartuja, Universidad de Granada, Granada 18071, Spain. Tel.: +34 958 249418; fax: +34 958 246186.
*E-mail address:* jmjramos@ugr.es

0166-4328/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.bbr.2012.08.036

temporal lobe and based on electrophysiological and lesion data, the perirhinal, postrhinal and entorhinal cortices, mainly, have also been critically involved in allocentric spatial memory in rats [20–23]. Especially relevant is the recent demonstration of spatially modulated neurons, the grid cells, in the dorsolateral band of the entorhinal cortex [24,25]. Consistent with electrophysiological data, lesion studies have shown the crucial involvement of the entorhinal cortex in the acquisition and retrieval of allocentric information [26,27]. Interestingly, under certain experimental conditions, the entorhinal cortex but not the hippocampus is necessary in spatial learning. Thus, during latent learning in a radial maze, the temporary inactivation of the dorsal entorhinal cortex during the unreinforced pre-exposure trials in a novel environment, impaired subsequent allocentric learning [28]; however, temporary hippocampal inactivation during the reinforcement-free spatial exploration, had no effect on subsequent spatial learning [29–32]. Secondly, outside the medial temporal lobe key regions have been identified involved in spatial processing, fundamentally the retrosplenial cortex [33,34], the parietal cortex [35,36], the cingulate cortex [37,38] and mammillary nuclei [39], mainly, all of which have a strong relationship with the hippocampus [40–43]. Furthermore, in parallel with the above studies in animals, a large number of investigations have now suggested the involvement of extrahippocampal regions in allocentric processing in human subjects [44–46]. Thirdly, in contrast with what the classic studies had initially proposed [1], under certain circumstances of training, hippocampal-lesioned rats can learn spatial locations in traditional paradigms of allocentric learning [47–51]. In our lab, using a reference spatial memory task in the radial maze, previous studies have shown that the introduction of an intramaze cue in the goal arm, completely eliminated the acquisition deficit in rats with hippocampal lesions [52].

Taken together, the above research suggests that under certain testing conditions the hippocampus does not seem essential for spatial learning, the rest of the navigational system being sufficient to construct a coherent allocentric representation that enables the rat to navigate toward a goal. However, it is not well known yet if the same conditions of training, in neurologically intact rats, are able to overcome the typical spatial retrograde amnesia observed when hippocampal lesions are made after the learning/training. Therefore, the goal of the present work was to investigate this possibility using our special training procedure. Specifically, a four-arm plus-shaped maze and a reference spatial memory paradigm were used, in which the goal arm was doubly marked: by an intramaze cue (a piece of sandpaper positioned on the floor of the arm) and by the extramaze constellation of stimuli around the maze. Experiment 1 showed an absence of anterograde amnesia when the above procedure was used but a profound anterograde impairment was detected when a standard procedure was used, based only on distal extramaze cues. Experiment 2 investigated the effect of hippocampal damage immediately after different groups of animals had learned the spatial task with the doubly marked or the standard procedure. In both conditions a profound retrograde amnesia was observed.

## 2. Materials and methods

### 2.1. Subjects

A total of 59 male Wistar rats from the breeding colony of the University of Granada (280–330 g at the time of surgery) were used in the following two experiments. Rats were housed singly and maintained on a 12:12 h light/dark cycle. Behavioral testing was performed during the light phase of the cycle. All experimental procedures were performed during the light phase of the cycle. All experimental procedures were performed in conformity with European (86/609/EEC) and Spanish (BOE 252, 2005) legislation and were approved by the Ethics Committee for animal research of the University of Granada (protocol number: 25-2005).

### 2.2. Surgery

Under the effects of sodium pentobarbital anesthesia (50 mg/kg ip, Sigma Chemical, St. Louis, MO), the rats were placed in a David Kopf stereotaxic apparatus with the incisor bar adjusted so that lambda and bregma were level. Rats were randomly assigned to either an experimental or a control group. The lesioned subjects received bilateral injections of NMDA (Sigma Chemical, PBS, pH 7.4, 0.07 M) through the insertion of a 30-gauge stainless steel cannula in eight sites of the dorsal hippocampus in relation to the interaural zero point [53]: AP = +5.9, L = ±1.6, V = +6.5; AP = +4.8, L = ±2.5, V = +6.5; AP = +3.8, L = ±3.2, V = +6.5; AP = +3.0, L = ±4.0, V = +5.4. The neurotoxin was administered in a 0.4 μl volume at each site through the cannula that was attached to a 5-μl Hamilton microsyringe. The solution was delivered with a Harvard Apparatus punp set (model 22, Holliston, MA) at an infusion rate of 0.1 μl/min. The cannula was left in situ for an additional 5 min before being withdrawn. The rats in the control groups underwent the same surgical procedure, except that vehicle was administered through the cannula. In experiment 1, the lesions were made 10 days before training; in experiment 2, however, hippocampal lesions were performed 1 day after the animals reached the acquisition criterion. Finally, lesions were made to the dorsal hippocampus instead of the whole hippocampus, because several studies have shown that the dorsal hippocampus is more important for spatial memory than the ventral hippocampus [54–57].

### 2.3. Apparatus

A four-arm plus-shaped maze was used. Each arm of the maze measured 60 cm in length × 10 cm in width and was connected to an octagonal central platform 35 cm in diameter. The walls of the central platform were made of transparent Plexiglas and were 15 cm in height. The walls of each arm were made of wood and measured 5 cm in height. The maze was 60 cm from the floor and a 200-W light bulb was hanging from the ceiling, 1.2 m above the center of the platform. The maze was located in an experimental room measuring 5.2 m × 5.3 m and on the walls there were various stimuli of different sizes, all well differentiated from each other.

### 2.4. Behavioral procedure

#### 2.4.1. Experiment 1: absence of anterograde amnesia for cued place learning

Previous data from our lab have shown that while hippocampal-lesioned rats learn about an intramaze cue, incidental allocentric processing also occurs [52]. Therefore, the objetive of this experiment was to replicate previous data obtained in our lab using a spatial reference task doubly marked and thus to compare, in the same experiment, these results with those obtained by other rats using a standard procedure. Based on previous data [52] we hypothesized that only the rats with hippocampal lesions trained under standard procedure will present anterograde amnesia, and not the lesioned rats trained using a cued place learning procedure. To investigate this matter, in the present experiment we used four groups of animals. In two group (standard groups; *n* lesion = 7, *n* control = 7) rats were trained in a reference spatial memory task using a standard procedure. After recovering from surgery, subjects were placed on a food-deprivation schedule to maintain them at 85–90% of their free-feeding body weight. Beginning the same day as the deprivation program, and for 7 successive days, all rats were handled daily for 10 min. The day after this period training began. Rats received eight trials per session, one session per day, until they reached the learning criterion, at least 14 correct trials (87%) on 2 consecutive days. At the beginnning of a trial, the four guillotine-doors separating the arms from the central platform were raised and the rat was placed at the end of one of the arms used for starting (south, north or east arms), with its back to the central platform. The order in which the different starting arms were used was randomized in each daily session. The reward, two 45-mg food pellets (P.J. Noyes, Lancaster, NH), was placed in the food cup located at the end of the west arm. The rat was considered to have made a choice when, having entered an arm, it crossed the halfway point with its four limbs. After a choice was made the guillotine-doors were lowered and the animal was left in the chosen arm for 10–12 s. The rat was then picked up and confined in a box for an intertrial interval of 30 s. Between trials, the maze was rotated 90° in a clockwise direction to prevent the rats from using olfactory signals to reach the goal arm. When the rats reached the learning criterion they were left in their respectives cages for 21 days and were not tested in any way. However, on day 21 the rats were tested in the same allocentric task used during the training. The retention session consisted of eight trials similar to those used during the training phase.

In the other two groups of rats (doubly marked or cued groups; *n* lesion = 8, *n* control = 7), the goal arm of the maze was doubly marked. First, throughout the acquisition period, a piece of sandpaper measuring 10 cm × 60 cm (80-grit) was positioned on the floor of the goal arm. Second, the extramaze constellation of stimuli in the experimental room continually guided the rats to the goal. To evaluate the incidental spatial learning in the doubly marked groups, each rat underwent a transfer test the day after reaching criterion. During this test, the intramaze cue was removed so that the only stimulus available to the rats to solve the test was the configuration of extramaze landmarks. The transfer test consisted of eight trials. The order in which the different starting arms were used was randomized, and it was the same for all the animals.

Download English Version:

https://daneshyari.com/en/article/6259447

Download Persian Version:

https://daneshyari.com/article/6259447

Daneshyari.com