Neurobiology of Learning and Memory 93 (2010) 415–421

Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

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

Prefrontal and hippocampal contributions to encoding and retrieval of spatial memory

John C. Churchwell [a,b], Andrea M. Morris [b], Nicholas D. Musso [b], Raymond P. Kesner [b,*]

[a] The Brain Institute, University of Utah, Salt Lake City, UT, USA
[b] Department of Psychology, University of Utah, Salt Lake City, UT, USA

ARTICLE INFO

Article history:
Received 3 August 2009
Revised 8 December 2009
Accepted 24 December 2009
Available online 13 January 2010

Keywords:
Prefrontal cortex
Orbitofrontal cortex
Hippocampus
Spatial
Navigation

ABSTRACT

The prefrontal cortex is thought to be critical for goal-directed action and the hippocampus is known to be importantly involved in spatial memory. Several studies have been suggestive of a role for the orbitofrontal cortex (OFC) in spatial navigation. However, the medial prefrontal cortex (mPFC) receives projections directly from the intermediate CA1 (iCA1) region of hippocampus and this link may be critical for spatial navigation. The purpose of the present investigation was to test the performance of rats receiving bilateral or disconnection infusions of lidocaine into OFC, mPFC, or iCA1 to determine the contribution of these structures to encoding and retrieval of spatial memory using the Hebb–Williams maze. A total of 92 male Long-Evans rats received chronic bilateral, contralateral, or ipsilateral implantation of cannulas into OFC, mPFC, or iCA1. Prior to testing on day 1 or day 2, subjects received central infusions of saline or lidocaine. The number of errors committed on the first five trials compared to the second five trials of day 1 was used to determine encoding, whereas retrieval was determined by comparing the second five trials of day 1 with the first five trials of day 2. The present findings suggest that mPFC and iCA1 are necessary and interact during encoding and retrieval; however, the OFC does not appear to be essential for either process. While the nature of the interaction between mPFC and iCA1 during encoding and retrieval is unclear, it may be supported by the integration of goals and spatial cues or strategy switching.

1. Introduction

The hippocampus (HPC) is well known for its role in spatial information processing and the prefrontal cortex (PFC) is regarded as necessary for guiding goal-directed action (Hasselmo, 2005; Miller & Cohen, 2001; O'Keefe & Nadel, 1978; Vertes, 2006). These structures likely interact under a variety of functional demands and such interactions may depend upon both memory process and content (Simons & Spiers, 2003). A number of models have specifically incorporated both the HPC and PFC into complex circuits involved in spatial navigation and interactions between these structures may be critical for optimal performance (e.g., see Mizumori, 2008).

The importance of the HPC in spatial navigation has long been recognized (O'Keefe & Nadel, 1978) and several studies in rodents have also been suggestive of a role for the orbitofrontal cortex (OFC) in spatial navigation (Corwin, Fussinger, Meyer, King, & Reep, 1994; Feierstein, Quirk, Uchida, Sosulski, & Mainen, 2006; Kolb, Sutherland, & Whishaw, 1983; Vafaei & Rashidy-Pour, 2004). However, the mPFC in rodents receives direct projections from the iCA1 region of the HPC and long-term potentiation (LTP) can be induced in the mPFC region through stimulation of iCA1 (Jay, Burett & Laroche, 1996; Jay & Witter, 1991). Further, enhanced place field stability and behavioral performance has been observed in mice under increasing attentional demands and lesions of mPFC alter place field activity in the HPC, suggesting an important relationship between these structures during spatial encoding (Kentros, Agnihotri, Streater, Hawkins, & Kandel, 2004; Kyd & Bilkey, 2003; Rowland & Kentros, 2008).

The prefrontal-hippocampal pathway has been proposed to be essential for integrating cognitive and emotional information necessary for adaptive action involving spatial information (Bast, 2007; Vertes, 2006). Specifically, studies using lesion and combined lesion/single-unit recording techniques have shown an important role for the intermediate hippocampus in spatial navigation and reward anticipation (Bast, Wilson, Witter, & Morris, 2009; Burton, Hok, Save, & Poucet, 2009). Neural recording studies in rodents have further demonstrated goal-related activity in the HPC and mPFC in spatial tasks (Hok, Save, Lenck-Santini, & Poucet, 2005; Hok et al., 2007).

Lesion studies have also shown that disruption of HPC or mPFC function impairs spatial navigation performance using the Hebb–Williams maze (Rogers & Kesner, 2006; Winocur & Moscovitch,

* Corresponding author. Address: Department of Psychology, 380 South 1530 East, Room 502, University of Utah, Salt lake City, UT 84112, USA. Fax: +1 801 581 5841.
E-mail address: ray.kesner@psych.utah.edu (R.P. Kesner).

1074-7427/$ - see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.nlm.2009.12.008

1990), a maze that has been used to study encoding and retrieval of spatial memory (Lee & Kesner, 2004; Rogers & Kesner, 2003; Vago, Bevan, & Kesner, 2007). A significant position has been attributed to the PFC and HPC for encoding and retrieval of spatial memory and the role of reinforcement and goal-directed action has been emphasized (Hasselmo, 2005; Muzzio, Kentros, & Kandel, 2009; Rolls & Kesner, 2006).

Prefrontal–hippocampal interactions have been examined using paradigms that test memory type, such as working or delayed memory (Floresco, Seamans, & Phillips, 1997; Jones & Wilson, 2005; Wang & Cai, 2006). Spatial navigation performance, as indexed by acquisition and retention on the Morris water maze, has also been used to examine prefrontal–hippocampal interactions (Wang & Cai, 2008). However, to our knowledge, no investigation has attempted to directly examine interactions between these structures for memory processes such as encoding and retrieval of information necessary for spatial navigation. Therefore, the present investigation sought to concurrently examine the role and interactions of OFC, mPFC, and iCA1 with an established measure of spatial encoding and retrieval in rats (Lee & Kesner, 2004; Rogers & Kesner, 2003; Vago et al., 2007). We utilized an inactivation procedure in order to control the timing of disruption associated with putative memory processes because lesion techniques can often leave open the question of what memory process is impaired. Moreover, crossed unilateral inactivation has been successfully employed to determine whether structural interactions are necessary for task performance and this procedure was also applied in the current study.

The present results suggest a simple dissociation between the mPFC and OFC during encoding and retrieval processes since bilateral inactivation of the mPFC, but not OFC, disrupted encoding and retrieval. The iCA1 has output directly to mPFC and bilateral inactivation of the iCA1 also produced impairments on both indices. Moreover, disconnection of iCA1 and mPFC also prevented encoding and retrieval, suggesting that these structures interact in both processes. Thus, the present investigation uniquely demonstrates both dissociations and interactions among prefrontal and hippocampal systems for encoding and retrieval of spatial information.

2. Materials and methods

2.1. Surgical procedure

All planned procedures and animal care were in accordance with the National Institute of Health and Institute for Animal Care and Use Committee guidelines and the Institutional Animal Care and Use Committee at the University of Utah. Ninety-two male Long-Evans rats weighing 250–350 g were housed in individual plastic containers and kept on a 12/12 light/dark cycle. Their weight was maintained at 80–90% of free feed weight with water available ad libitum. Prior to surgery, subjects were deeply anesthetized using isoflurane gas, placed in a sterotaxic apparatus with a continuous flow of isoflurane, and prepared for the surgical procedure by applying a surgical drape and betadine antiseptic to the surgical site. An incision was made in the skin above the skull. The skin was retracted and burr holes were drilled in the skull to receive stainless-steel anchor screws and provide access to the regions intended for cannulation. Cannulas were inserted at the following coordinates: OFC: 3.0 mm anterior to bregma, ±3.2 mm lateral from midline, 4.2 mm ventral from dura; mPFC: 25° from midline, 3.0 mm anterior to bregma, ±2.0 mm lateral from midline, 4.6 mm ventral from dura; iCA1: 5.8 mm posterior to bregma, ±5.3 mm lateral from midline, 3.4 mm ventral from dura. Cranioplastic cement was applied around cannulas and screws to chronically anchor the cannulas in place. In experiment 1, subjects were implanted with cannulas bilaterally in either mPFC, OFC, or iCA1. In experiment 2, subjects were implanted with cannulas in mPFC and iCA1 unilaterally in contralateral hemispheres or within a single hemisphere.

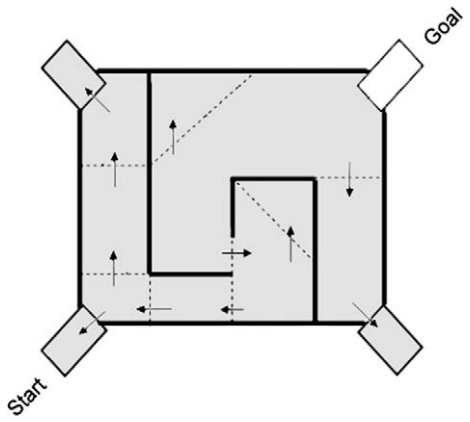

Fig. 1. Shows the modified Hebb–Williams maze with error zones indicated by dashed lines. Arrows show the direction of travel for error zone entries to be counted as errors (i.e., travelling away from the goal). There were a total of 11 error zones including reentry into the start box or other non-goal boxes.

2.2. Behavioral apparatus

The maze was surrounded by six 3-dimensional (3-D) cues hanging from the walls. The overall design of this Hebb–Williams maze was intended to increase dependence on the 3-D extra-maze cues for navigation. The maze itself was constructed from 1.9 cm thick wood and painted gray with a uniform grid pattern of holes drilled in the floor every 15 cm (Fig. 1). The floor of the maze was 72.6 × 72.6 cm. The walls were constructed of clear plexiglass (25 cm high and .6 cm) and had a black painted strip rising 7.5 cm from the bottom. Four wooden boxes were located at each corner of the maze (13 cm wide × 25 cm long × 17.5 cm high). Two of the boxes were used as the fixed start and goal locations.

2.3. Behavioral task and experimental design

Initially subjects were habituated to handling for 5–10 min each day over the course of 5 d. After habituation, subjects were trained to run back and forth on a wooden linear track with start and goal boxes at each end containing food rewards (Froot Loop cereal; Kellogg, Battle Creek, MI). During the first 2 d of runway training, 8–10 cereal pieces were placed along the runway and in the goal boxes and subjects were allowed to freely move along the runway and consume the food rewards. Following the shaping procedure, gates were introduced in front of each shuttle box and a food reward (~0.5 Froot Loop) was placed in the box opposite the subject. The gates of the shuttle box were removed and the subject was allowed to traverse the runway to obtain the cereal. The gate was then closed behind the subject and the opposite shuttle box was baited and the procedure was continued in the same manner. Subjects received 10 daily trials of runway training for five to 6 d. Following acquisition of runway training, surgery was performed to implant cannulas. After fully recovering from surgery, subjects received three further days of runway training prior testing on the maze. Each subject received surgical bilateral, contralateral, or ipsilateral cannulation of the mPFC, OFC, or iCA1. Since bilateral inactivation of mPFC and iCA1 led to impairments, another experiment was also carried out using contralateral and ipsilateral cannulation of mPFC and iCA1. There were three treatments in the first experiment involving bilateral mPFC, OFC, and iCA1: (1) saline – day 1