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Short communication

A role for the head-direction system in geometric learning

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ABSTRACT

Several recent models of episodic memory have highlighted a potential contribution from the head-direction system; there is, however, surprisingly little known about the behavioural effects of selective lesions within the head-direction system. To address this issue, and determine what aspects of spatial memory are dependent on the head-direction system, rats with selective lateral mammillary body lesions were tested on tasks that required the use of specific spatial cues, including direction, visual allocentric, and geometric cues. Animals were first tested on a modified version of the T-maze alternation task that enabled the systematic removal of intramaze and visual allocentric cues. Rats were next tested on a geometric task that required the use of the shape of the environment to locate a hidden platform in the water-maze. The lesion rats were impaired on one stage of the T-maze alternation task and on the acquisition of the geometric task; these results are consistent with the head-direction system contributing to the processing of, and/or subsequent use, of visual allocentric and geometric cues. From the pattern of impairments it also appears that, with training, rats with lateral mammillary body lesions are able to recruit other navigational systems or that there is some degree of redundancy within the head-direction system.

1. Introduction

Although recent models of episodic memory formation have highlighted a potential contribution from the head-direction system [1,2], there are very few behavioural studies that have specifically addressed this possibility. Interest in the head-direction system has recently increased as it is the first of the spatial representation systems (i.e., head-direction cells, place cells, grid cells) to show adult-like properties [3,4] and is, therefore, potentially important for the subsequent maturation of the other navigational systems.

The present study focused on one component of the head-direction system, the lateral mammillary nucleus (LMN). This structure occupies a pivotal position within the head-direction system [5,6] and, via its interactions with the dorsal tegmental nucleus of Gudden, is responsible for the head-direction signal in the anterodorsal thalamic nucleus (ADN) [5,7,8] and postsubiculum [9]. However, to date, only one study has examined the behavioural effects of selective LMN lesions [10] and none has assessed lesions confined to the ADN, although there are behavioural studies where the lesions are centred on the ADN with varying amounts of additional thalamic damage [11–13].

The aim of the present study was to determine how the head-direction system contributes to spatial memory; more specifically, whether the head-direction system is required for mnemonic tasks that require the use of specific spatial cues, including allocentric, directional and geometric cues. These spatial cues were chosen on the basis of the electrophysiological properties of head-direction cells (e.g., [6,14]). Rats with LMN lesions were first tested on a variation of the T-maze alternation task where it is possible to eliminate systematically the cues available to perform the task. Subsequently, LMN lesion rats were tested on a task that required animals to use geometric cues, e.g., shape of the environment, to navigate to a hidden platform. This task is sensitive to anterior thalamic lesions [12] and lesions of the hippocampal formation [15] while fornix lesion rats are unimpaired on this task [12]. It is, therefore, possible the lesion-induced deficits on this task reflect the loss of the ascending head-direction information from the LMN.

Twenty-one male, pigmented DA (Dark Agouti) rats (220–250 g; Harlan, Bicester, UK) were used in the study. All experiments were performed in accordance with the UK Animals (Scientific Procedures) Act (1986) and associated guidelines. Animals were anaesthetised with sodium pentobarbital (60 mg/kg) and placed in a stereotaxic headholder (David Kopf Instruments, Tujunga, CA) with the incisor bar set at +5.0 mm. Injections of 0.30 μl of 63 mM ibotenic acid (Biosearch Technologies Inc., San Rafael, CA, USA) in phosphate buffered saline (PBS) at pH 7.2 were made in one site per hemisphere using a 1 μl syringe (Hamilton, Switzerland); injections were made over 10 min and the needle was left *in situ*

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for a further 5 min. The stereotaxic coordinates were: anterio-posterior, −2.2 mm from bregma; medio-lateral, ±1.0 mm from the midline; dorso-ventral, −9.2 mm from the top of the dura. The surgical controls underwent the same procedure with the needle being lowered but no injection was made. After surgery, the skin was sutured together and antibiotic powder was applied to the wound (Acramide, Dales Pharmaceuticals, UK). Animals received 5 ml glucose saline subcutaneously and then placed in a temperature-controlled recovery box. Paracetamol (for pain relief) and sucrose were added to the rats' drinking water for three days post-surgery.

It was imperative that the LMN lesions did not encroach into the medial mammillary nucleus as this is known to be important for spatial memory [see 16]; the lesions were, therefore, deliberately discrete and, as intended, none of the lesions extended into the medial nucleus (Fig. 1). However, in order to meaningfully interpret any null effects it was necessary for there to be considerable cell loss in LMN across both hemispheres [7]. Five cases that had appreciable unilateral or bilateral LMN sparing were, therefore, removed from further analyses. The final numbers were: LMN lesion rats (LMNx), $n = 7$ and surgical controls (Sham), $n = 8$ for T-maze alternation, $n = 7$ for the geometric task as a surgical control was sacrificed due to a medical complication unrelated to the experiment.

For the T-maze alternation task, the same apparatus and testing procedures were used as previously described [17,18]. Briefly, two identical cross-mazes were used during the experiment (Fig. 2a), either individually (Stage 1), or placed side-by-side (Stages 2–3); a barrier was used to block access to the arm opposite the start arm, effectively transforming it into a T-maze. Three weeks after surgery, and one week prior to the start of the experiment, the animals were placed on food-restriction; their weight did not fall below 85% of their free feeding weight. Pre-training consisted of five days of maze habituation during which reward pellets (45 mg; Noyes Purified Rodent Diet) were placed in a sunken food well at the end of the arm; the pellets were continuously replaced so that no arm was found to be empty on return. The rats were equally habituated to both mazes.

Rats received eight trials per daily session; each trial consisted of a forced 'sample' run followed by a 'choice' run (Fig. 2a). During the forced sample run, one of the side arms of the maze was blocked using an aluminium barrier. After the rat turned into the pre-selected arm, it was allowed to eat the two reward pellets. The

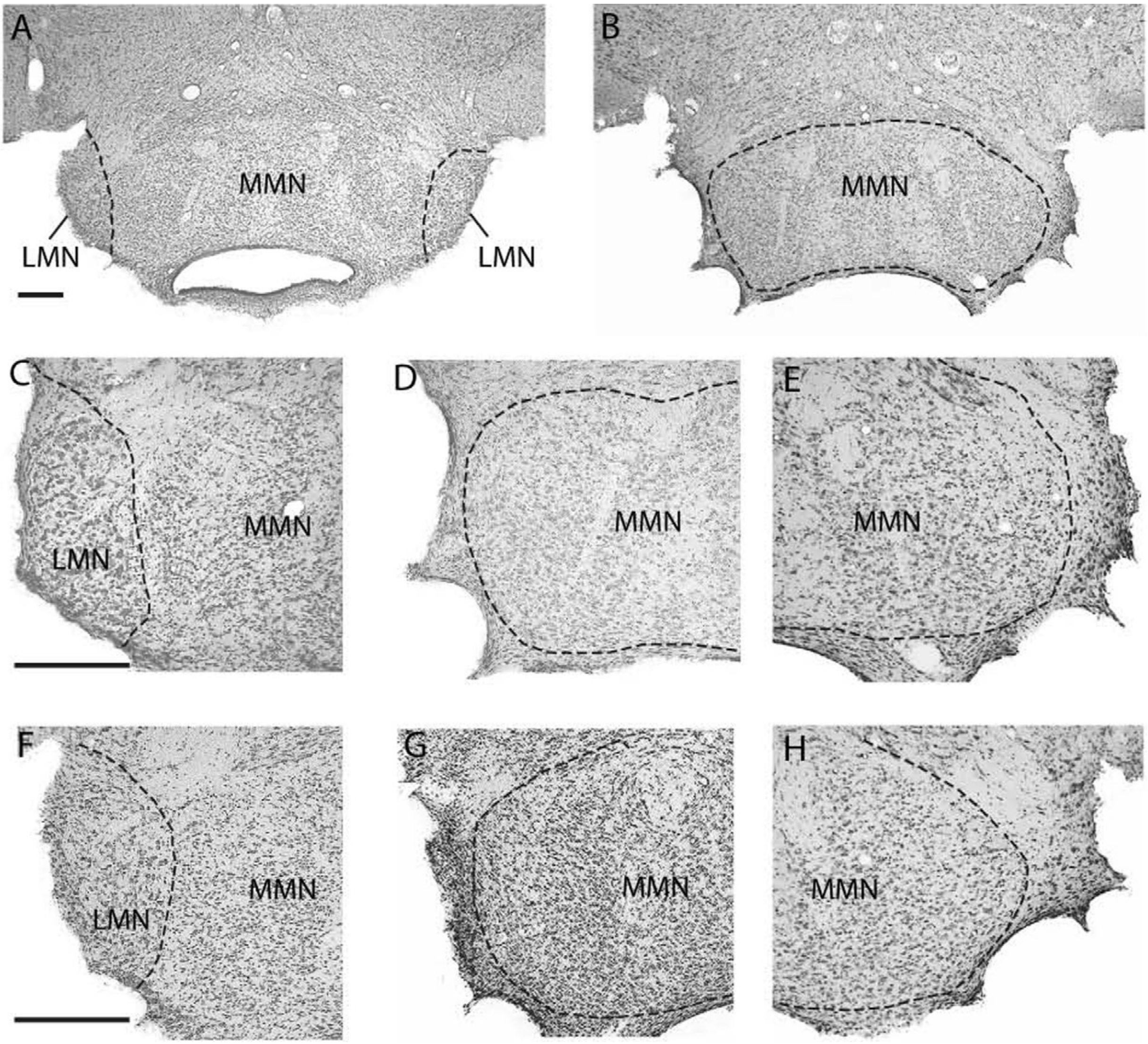

Fig. 1. Photomicrographs of the lateral mammillary nuclei lesions. The borders of the lateral mammillary nuclei are indicated with a black dashed line in the surgical controls (A, C, F) and the borders of the medial mammillary nuclei are indicated with a black dashed line in the lesion animals (B, D, E, G, and H). The photomicrographs labelled B, D, E, G and H depict the lesions in two animals (included in the analyses) with the greatest (B, D, E) and least (G, H) amount of tissue sparing. Scale bars: 0.25 mm. *Abbreviations*: LMN, lateral mammillary nuclei; MMN, medial mammillary nuclei.