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Dentate gyrus supports slope recognition memory, shades of grey-context pattern separation and recognition memory, and CA3 supports pattern completion for object memory ☆

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A B S T R A C T

In order to examine the role of the dorsal dentate gyrus (dDG) in slope (vertical space) recognition and possible pattern separation, various slope (vertical space) degrees were used in a novel exploratory paradigm to measure novelty detection for changes in slope (vertical space) recognition memory and slope memory pattern separation in Experiment 1. The results of the experiment indicate that control rats displayed a slope recognition memory function with a pattern separation process for slope memory that is dependent upon the magnitude of change in slope between study and test phases. In contrast, the dDG lesioned rats displayed an impairment in slope recognition memory, though because there was no significant interaction between the two groups and slope memory, a reliable pattern separation impairment for slope could not be firmly established in the DG lesioned rats. In Experiment 2, in order to determine whether, the dDG plays a role in shades of grey spatial context recognition and possible pattern separation, shades of grey were used in a novel exploratory paradigm to measure novelty detection for changes in the shades of grey context environment. The results of the experiment indicate that control rats displayed a shades of grey-context pattern separation effect across levels of separation of context (shades of grey). In contrast, the DG lesioned rats displayed a significant interaction between the two groups and levels of shades of grey suggesting impairment in a pattern separation function for levels of shades of grey. In Experiment 3 in order to determine whether the dorsal CA3 (dCA3) plays a role in object pattern completion, a new task requiring less training and using a choice that was based on choosing the correct set of objects on a two-choice discrimination task was used. The results indicated that control rats displayed a pattern completion function based on the availability of one, two, three or four cues. In contrast, the dCA3 lesioned rats displayed a significant interaction between the two groups and the number of available objects suggesting impairment in a pattern completion function for object cues.

1. Introduction

1.1. Pattern separation

With respect to pattern separation process (Rolls, 1996) model proposed that pattern separation is facilitated by sparse connections in the mossy fibre system, which connects dDG granular cells to dorsal dCA3 pyramidal neurons. Separation of patterns is accomplished based on the low probability that any two dCA3 neurons will receive mossy fibre input synapses from a similar ensemble of dDG cells. Mossy fibre inputs to dCA3 from dDG are suggested to be essential during learning and may influence which dCA3 neurons fire based on the distributed activity within the dDG. Cells of the dDG are suggested to act as a competitive learning network with Hebb-like modifiability to reduce redundancy and produce sparse, orthogonal outputs. If disruption of dDG function results in inefficient pattern separation, then deficits involving spatial tasks may occur when there is increased overlap or similarity among distal cues and presumably increased similarity among representations within the dDG. Remembering a specific location in, for example, an eight-arm maze, a water maze, dry-land version of the water maze or a spatial context in fear conditioning maybe influenced by the degree of overlap among critical distal spatial cues. Two important features must be fulfilled by research into

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☆ All coauthors agree to having their names listed as authors and that all colleagues whose unpublished work is referred to, or who are acknowledged, agree to that.

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pattern separation processes. The first is that there should be a parametric alteration of interference among a designated set of stimuli (e.g. spatial locations, visual objects), and the second is the need for a function of behavioural responses that scales with interference among the selected stimuli (e.g. spatial locations, visual objects). It is also important that tasks evaluating pattern separation be encoding tasks – since pattern separation, by definition, is the process by which information is encoded in such a manner to minimize interference among memory representations/stimuli and facilitate later recall.

1.2. Pattern completion

During retrieval of information, Marr (1971) suggested that the hippocampus recurrent collaterals should play a major role in the hippocampus in retrieving originally stored information patterns in the face of partial inputs to the hippocampus ("collateral effect" or pattern completion). McNaughton and Morris (1987) and Rolls and Treves (1998) suggested that an autoassociative network within dCA3 should be able to support pattern completion. There are two important features that must be fulfilled by research into pattern completion processes: The first, there should be parametric alteration of the number or degree of degradation to retrieval cues (e.g. spatial locations, visual objects) and the second, there is a need for a function of responses that scales with this degradation. It is also important that tasks evaluating pattern completion be retrieval tasks – since pattern completion, by definition, is the process by which a degraded retrieval cue results in recall for a previously stored memory trace.

2. Experiment 1: A role for the dorsal dentate gyrus in slope (vertical space) context recognition memory

It has been suggested that the dorsal dentate gyrus (dDG) supports the processing of spatial information and spatial pattern separation (for a review see Kesner, 2013). Also, within space a small proportion of cells (2–3% cells) in the dDG display place cells and often multiple places within a place cell (Jung & McNaughton, 1993; Leutgeb, Leutgeb, Moser, & Moser, 2007). Furthermore, dDG cells respond to novelty (Nitz & McNaughton, 2004). A number of researchers examining vertical space using a climbing wall pegboard and a vertical helix (a spiral stairway) have recorded place cells in dCA1 (Hayman, Verriotis, Jovalekic, Fenton, & Jeffery, 2012; Savelli & Knierim, 2011), but there have not been any recording of dDG granule cells in the context of vertical space. Also, there have not been any studies of pattern separation for vertical space. Previous research has shown that rats can discriminate a 10 degree vertical space (slope) (Miniaci, Scotto, & Bures, 1999) and that the threshold for detection of slope in Long Evans rats is 17 degrees (Russell & Pereira, 1981). Thus far, there are no studies that have examined the dDG in supporting pattern separation for vertical space. Thus, the aim of Experiment 1 is to determine whether the dDG supports slope recognition memory and pattern separation for degrees of angle changes for slope recognition memory.

3. Material and methods

3.1. Rats

Thirteen male Long-Evans rats weighing 250–350 g were housed in individual plastic containers and kept on a 12/12 light/dark cycle. Food and water were available ad libitum.

3.2. Surgical procedures

The rats were randomly placed into three separate groups: a dDG lesion group which received bilateral colchicine lesions ($n = 6$), a sham surgery control group ($n = 3$) and a non-operated control group ($n = 4$). Each animal was anesthetized with isoflurane and then injected with atropine sulphate to reduce salivation. Isoflurane was also used to maintain anesthesia (2–4% in 2 L/min medical air). Each rat was placed in a stereotaxic instrument (Kopf Instruments, Tujunga, CA) with its head level. An incision along the midline of the scalp was made to expose the skull and Bregma. Four small burr holes, two on either side, were drilled through the skull and injections of colchicine (2.5 mg/ml, .33 μl/min) at a volume of 0.08 μL/site were made into two dorsal DG sites per hemisphere using the following coordinates: 2.7 mm posterior to bregma, 2.1 mm lateral to midline, 3.4 mm ventral from dura and 3.7 mm posterior to bregma, 2.3 mm lateral to midline, 3.0 mm ventral from dura. All lesion coordinates were based on Paxinos and Watson's (2009) stereotaxic atlas of the rat brain. For all injections, the injection cannula remained in place for at least 1 min after the injection to allow for diffusion. The coordinates for the sham lesions were carried out in the same manor, but physiological saline was substituted for the colchicine. Following surgery, the incision was sutured. Rats were placed back in their home cage immediately after surgery. While recovering they were provided Carprofen (4 mg/kg) for seven days. All protocols were performed in concordance with the NIH Guide for the Care and Use of Laboratory Animals and the Institutional Animal Care and Use Committee (IACUC) at the University of Utah.

3.3. Apparatus

Testing was conducted in a transparent plastic box (93 cm long, 93 cm wide and 64 cm high) in a quiet testing room. The bottom of the box stood 57 cm above the floor. The floor of the box was covered by three parallel boards (93 cm long, 41 cm wide, and 0.4 cm thick) made of wood and rubber. The middle board was always flat, with the other two boards sloping up at angles from the middle board to the walls of the box. These angles were controlled by placing sets of four wooden blocks under the two sideboards. The slope of each sideboard was stable because all four wooden blocks in each set were the same height. In addition, the boards were covered by wire netting, providing traction, making it easy for the subjects to either move about or stay in place. There were 20 wooden blocks used in the experiment. All the wooden blocks had the same base cross-sectional area (8 cm long, 5 cm wide), and the blocks varied in height. Eight of the wooden blocks were 6.7 cm high. Four of them were 12 cm high. The other eight of them were 16.5 cm high. When placed under a sideboard the 6.7 cm blocks produced an angle of 10 degrees, the 12 cm blocks produced an angle of 20 degrees and the16.5 cm blocks produced a 30-degree angle. In addition, a 40-degree angle was produced by placing some of the 16.5 cm blocks on top of other blocks that had been placed on their sides as illustrated in Fig. 1 for study phase and Fig. 2 for test phase.

3.4. Behavioural task and experimental design

All behavioural testing commenced at earliest ten days post operation, which allowed ample time for recovery. Prior to testing, the angle of the slope on each of the two sideboards was set. In the study phase, once a subject was placed on the board in the middle of the box, two stopwatches, one for each sideboard, were used to record the respective time that the rat spent exploring each of the side boards. An additional stopwatch was used to time the study phase. After five minutes, the rat was returned to its home cage for 10 min. During that time, the slope of one sideboard was