

A study of remote spatial memory in aged rats

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Abstract

The effect of aging on remote spatial memory was tested in a group of 2-year-old rats (VR-O) that, as young adults, were reared for 3 months in a complex 'village' environment. The VR-O rats exhibited significant savings in finding the locations of specific reward compartments within the village, relative to a group of old rats (VNR-O) experiencing the village for the first time. The VNR-O rats were also impaired, relative to naive young rats, in learning the reward locations. Probe tests indicated that the VR-O rats retained allocentric spatial memory for the environment and were not using sensory or other non-spatial cues to guide behaviour. Overall, the results indicate that the aged rats experienced a decline in the ability to learn and remember detailed spatial relationships and that the VR-O group's successful performance on the remote spatial memory test was guided by a form of schematic memory that captured the essential features of the village environment. The potential contribution of the hippocampus to the pattern of lost and spared learning and memory observed in the aged rats was discussed. © 2008 Elsevier Inc. All rights reserved.

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1. Experiment 1

Spatial memory, based on the ability to form and remember allocentric spatial relationships in a complex environment, is known to be particularly vulnerable to the effects of normal aging in animals and humans (Barnes, 1979; Light, 1983; Park et al., 1983; Gallagher and Pelleymounter, 1988; Moffat et al., 2006). The loss of spatial memory in old age is related to failures in recalling contextually bound episodic events and has been attributed to changes in the hippocampus, a brain region that is functionally linked to spatial information processing (O'Keefe and Nadel, 1978; Maguire et al.,

1996; Rosenbaum et al., 2001) and one of the first structures to show significant deterioration as part of the aging process (Gallagher et al., 1995; Geinisman et al., 1995; Winocur and Gagnon, 1998).

Although there has been considerable research into age differences in spatial memory, the focus has been mainly on recently experienced events, with scant attention paid to effects of age on recalling very old or remote spatial memories. To our knowledge, this issue has not been investigated systematically in humans, and there appears to be only one relevant report in the animal literature (Beatty et al., 1985). These investigators tested spatial learning and memory in a radial arm maze, a task that is known to be sensitive to the effects of aging, as well as hippocampal lesions. The results showed that 26-month-old rats, trained on the radial arm maze 2 years earlier, performed significantly better than old rats administered the task for the first time. It should be noted that

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this study did not test remote memory for spatial locations and what appeared to be preserved was a working memory strategy in a spatial context.

There are numerous challenges to assessing remote spatial memory in old age. For example, it is necessary to exert strict control over the subjects' experience with the environment, while ensuring that the experience was adequate to allow the formation of memory representations that can support accurate recall after very long intervals. As well, it is important that subjects have no contact with the environment between the original experience and remote memory testing. These factors are taken into account in a recently developed test, used initially to assess spatial memory in rats with hippocampal lesions (Winocur et al., 2005). In that test, young adult rats are reared socially in a complex environment ('village') that contains desirable reward objects (e.g., food, water) in different locations. Following an interval, the animal's ability to find specific rewards is assessed as a test of spatial memory.

In Experiment 1, the village paradigm was used to investigate remote spatial memory in aged rats under conditions that model those in effect when elderly humans attempt to remember specific locations learned a long time ago but were not experienced subsequently. Two groups of old rats – one reared for 3 months as young adults in the village and the other experiencing the village for the first time – were tested on their ability to find specific reward locations in the village. At test, rats reared in the village performed significantly better than naive old rats that were also impaired relative to a group of young rats exposed to the village for the first time. Additional testing in Experiment 2 showed that the reared rats were not guided by internal or external sensory cues but, rather, by a map-like allocentric spatial representation of the environment that they had acquired through their early experience in the village.

1.1. Method

1.1.1. Subjects

Sixteen, male Long-Evans rats, approximately 23 months of age at the beginning of the experiment, participated in the research. The rats were acquired as young adults from Charles River laboratories in St. Constant, Quebec, and reared in the Trent University animal facility. Throughout the present study, the rats were maintained on 12:light/12:dark cycle, with all testing conducted during the dark phase of the cycle. Throughout testing, rats were placed on a 23 h food- or water-deprivation schedule, depending on the incentive condition to which they were assigned.

The study was approved by the Trent University Animal Care Committee and the rats were regularly examined by a veterinarian.

1.1.2. Apparatus

The village (1.2 m × 1.2 m × 1.2 m), shown in Fig. 1, was located in the centre of a room with standard laboratory furni-



Fig. 1. The complex 'village' environment.

ture (e.g., desks, book shelves) and pictures on the walls. The room was dimly and uniformly illuminated by overhead lightings. The village contained two levels, with interconnected walkways within and between the levels. Two walkways leading to the lower levels were situated across from the entrance to the reward compartments in the north-east and south-west corners. The walls and ceiling were made of wire mesh, and the walkways of aluminum sheet metal. The upper level, also constructed of sheet metal, consisted of a gathering area in the middle of the upper level with four walls each containing a central opening. This area served as a start box for training and test trials. A compartment containing food (south-east corner), water (north-west corner), an assortment of toys (north-east corner), or a female rat (south-west corner), was attached to each of four corners on the lower level. The compartment containing the female rat was separated from the village by a wire mesh screen, whereas the other compartments could be entered freely.

1.1.3. Procedure

Old rats were assigned to the Village-Reared (VR-O, $N=4$) or the Village-Non-reared (VNR-O, $N=12$) condition.

1.1.3.1. VR condition. Rats in the VR-O condition originally participated as part of a control group in our investigation of the effects of hippocampal lesions on spatial memory conducted almost 2 years earlier (Winocur et al., 2005). The VR-O rats were 3 months old at the beginning of that study and about 8 months old upon completion. For the first 3 months of that study, the VR-O rats spent 8 h/day in the village during the high-activity part of their diurnal cycle. During these sessions, the rats were allowed to explore the entire village, with access to all the reward sites, which were always in the same locations. After each session, the rats were returned to individual cages, where they were deprived of food and water.

At the end of the 3-month village exposure period, the VR-O rats (as young adults) were maintained on food or water

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