Behavioural Brain Research 285 (2015) 89–98

Contents lists available at ScienceDirect

Behavioural Brain Research

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

Research report

The influence of context on recognition memory in monkeys: Effects of hippocampal, parahippocampal and perirhinal lesions

Jocelyne Bachevalier*, Sarah Nemanic[1], Maria C. Alvarado[2]

Department of Neurobiology and Anatomy, University of Texas Health Science Center, Houston, TX, USA

HIGHLIGHTS

- Control animals showed weaker contextual memory after a context change.
- Hippocampal lesions alter contextual memory.
- Perirhinal cortex lesions alter contextual memory.
- Parahippocampal lesions alter contextual memory.

ARTICLE INFO

Article history:
Received 2 June 2014
Received in revised form 3 July 2014
Accepted 6 July 2014
Available online 12 July 2014

Keywords:
Visual Paired Comparison
Contextual memory
Rhesus monkey
Contextual binding

ABSTRACT

This study further investigated the specific contributions of the medial temporal lobe structures to contextual recognition memory. Monkeys (*Macaca mulatta*) with either neurotoxic lesions of the hippocampus, aspiration lesions of the perirhinal cortex and parahippocampal areas TH/TF, or sham operations were tested on five conditions of a visual-paired comparison (VPC) task in which 3-dimensional objects were presented over multicolored backgrounds. In two conditions (Conditions 1 and 2: Context-changes), the sample object was presented on a new background during the retention tests, whereas in the three others (Conditions 3–5: No-context-changes) the sample object was presented over its familiar background. Novelty preference scores of control animals were weaker, but still significantly different from chance, in the Context-changes conditions than on the No-context-changes conditions. Animals in the three experimental groups showed strong preference for novelty on the No-context-change conditions, but weaker novelty preference on the Context-change conditions than controls. Thus, animals in all three lesion types had greater difficulty recognizing an object when its background was different from that used during encoding. The data are consistent with the view that the hippocampal formation, areas TH/TF, and perirhinal cortex contribute interactively to contextual memory processes.

1. Introduction

Context refers to the general information that is associated with a specific stimulus at the time of encoding. It includes the environment in which it occurs, the place where it is located (spatial context) and the time during which it happens (temporal context). Thus, context can be anything associated with the to-be-remembered item in an event, and as such, can vary substantially in its complexity. It can be as simple as the color of text on a word list, or as complex as the physical environment in which learning took place. Several studies in humans have demonstrated a decreased memory performance when context is changed between encoding and retrieval after changing semantic [48,77,87,90], cue specific [17,42,69,70,80,84], olfactory [13], auditory [37] or environmental [12,27,82,84] contexts. Further, both rodent [19,21, 83] and primate [73] studies have shown that, although animals are able to recognize objects in a changed background context, recognition memory was stronger when the familiar context was used in the retrieval phase. Thus, as in humans, recognition memory processes in animals are also modulated by memory for contextual information.

The study of the neural substrates responsible for contextual memory has received increased attention in the last decade as a result of recent theoretical considerations of the role of the medial

* Correspondence address: Yerkes National Primate Research Center, 954 Gatewood Road, Atlanta, GA 30329, USA. Tel.: +1 404 727 9765; fax: +1 404 727 8088.
E-mail addresses: jbachev@emory.edu (J. Bachevalier), sarah.nemanic@oregonstate.edu (S. Nemanic), malvara@emory.edu (M.C. Alvarado).
[1] Present address: College of Veterinary Medicine, Oregon State University, 700 SW 30th Street, Corvallis, OR 97331, USA. Tel.: +1 541 737 4812.
[2] Present address: Yerkes National Primate Research Center, Emory University, Atlanta, GA. Tel: +1 404 727 8017.

http://dx.doi.org/10.1016/j.bbr.2014.07.010
0166-4328/© 2014 Elsevier B.V. All rights reserved.

temporal lobe (MTL) structures in memory. There is general agreement that, within the MTL, the hippocampus acts in concert with the parahippocampal and perirhinal cortex to support recognition memory. In this view, the hippocampus associates (or binds) contextual information from the parahippocampal cortex with object representations from the perirhinal cortex, and encodes and maintains relationship among stimuli [18,20,25,26,58,88]. There exists growing evidence to support the role of the hippocampus and parahippocampal cortex in contextual memory, although the role of the perirhinal is still debated.

Evidence of the role of the hippocampus in contextual memory comes from both human and animal studies. Patients with amnesia resulting from either Korsakoff's syndrome or MTL damage were not able to benefit from the use of temporal [71], semantic [56] or visual [14] contextual cues during memory tasks and showed impaired performance as compared to control subjects. This impairment is also reported in patients with more selective bilateral hippocampal lesions or with left unilateral hippocampal damage [43,85,86]. The effect of context information on memory performance is also exemplified in neuroimaging studies of normal subjects indicating hippocampal activations during either recognition of contextual information associated with objects [8,79] and with words [54], or after changes in context surrounding a stimulus [22]. Similarly, fornix transections impaired memory performance when stimuli were either complex naturalistic scenes [32,34], or objects embedded in complex scenes [33], and hippocampal lesions impaired recognition memory performance when a change of context occurred between encoding and retrieval [24,45,60,73,75]. Impaired memory was also found in a contextual discrimination task where the background context signaled the rewarded object [78] and in a discrimination task for which the use of contextual background information enhanced memory performance [23]. Hippocampal place fields and neuronal responses to task-relevant stimuli are also highly sensitive to changes in the context, even when the contexts are defined by abstract task demands rather than the spatial geometry of the environment, suggesting that place fields reflect a more general context processing function of the hippocampus (for review see [47,53,81]). Finally, molecular activation studies revealed that initial introduction of rats into a novel environment or in an environment different from that used in the exploration phase increases *c-fos* activation or Arc mRNA levels in the hippocampal formation [39,76,91]. Thus, there exists substantial evidence for a contribution of the hippocampus in forming contextual memory representations.

Recent neuroimaging studies in humans have also implicated the parahippocampal cortex in contextual memory either during scene processing [29–31,46,61], object identification [4], intentional retrieval of visual context information [40] or familiarity-based recognition [41,55]. In addition, activations of the hippocampus and parahippocampal cortex have been reported in humans during binding operations between objects and context [38]. More recently, Howard et al. (2011) provided compelling evidence that the parahippocampal cortex supports neural representations of the global context within which events occur, whereas the hippocampus plays a more specific role in the rapid creation of item-context bindings. Similarly, animal lesion studies have demonstrated that the postrhinal cortex in rodents (homologous to the parahippocampal cortex in primates; [9]) is critical for learning about the within-scene position or context [24,65]. Finally, molecular activation studies in rodents revealed elevated *c-fos* in the postrhinal cortex when the environmental context was changed between study and test [91]. Thus, there is a growing support for a role of the parahippocampal cortex in contextual recognition memory.

Studies investigating the contribution of the perirhinal cortex in contextual recognition memory have given contradictory results. For example, damage to the perirhinal cortex in monkeys impaired the learning of complex scenes [33] and object identification when the objects were embedded in complex scenes [7]. In contrast, using a spontaneous object recognition paradigm, Norman and Eacott [65] reported that animals with perirhinal cortex were unimpaired on memory for object in context. Similarly, changing the environment between study and test in a recognition task did not lead to any change in *c-fos* activation in the perirhinal cortex [91]. Thus, the evidence so far suggests that the hippocampus and parahippocampal cortex, but not the perirhinal cortex, may be more importantly involved in contextual memory processes. Nevertheless, one shortcoming of these process-specific dissociations from animal studies is that they are mostly derived from comparing findings across studies that varied widely in the specific structures damaged (some compared perirhinal/hippocampus, others compared hippocampus/parahippocampal cortex) and the types of behavioral paradigms used to assess memory (problem-solving task versus incidental memory task). Furthermore, extent of damage could also be a potential confounding factor. For example, in our earlier studies [73] using a visual paired-comparison task in which backgrounds onto which objects were presented changed between encoding and retrieval, animals with neonatal hippocampal lesions showed a significant decrease in novelty preference as compared to controls; however, the hippocampal lesions were performed by aspiration procedures and extended to include the parahippocampal cortex, such that the effects of lesions on memory performance could not be solely ascribed to the hippocampal damage.

Thus, the aim of the present study was to directly compare the effects of selective damage to the hippocampus, parahippocampal cortex, and perirhinal cortex in monkeys on contextual memory using an incidental recognition memory task. The visual paired-comparison (VPC) task was modified so that the backgrounds onto which objects were presented were changed between the familiarization (or encoding) phase and the retention (or retrieval) phase.

2. Method

2.1. Subjects

Subjects were eighteen rhesus monkeys (*Macaca mulatta*) of both sexes. Six monkeys (all male) received selective ibotenic acid lesions of the hippocampal formation (Group H), three monkeys (1 male and 2 females) received aspiration lesions of the perirhinal cortex (Group PRh), three (3 males) received aspiration lesions of areas TH/TF of the parahippocampal gyrus (Group TH/TF) and six (all male) were sham-operated controls (Group C). Subjects weighed 5–12 kg and were aged 3–12 years at the time of testing. They were housed individually, fed *ad libitum* Purina Monkey Chow and water, and were maintained on a 12-h light:12-h dark cycle. Monkeys were given multi-vitamins daily and fresh fruit weekly. There were no food or water manipulations.

Monkeys in Groups PRh and TH/TF were tested on Transverse Patterning, Object VPC, Spatial VPC, DNMS and dDNMS before beginning the present experiment [2,3,64]. Monkeys in Groups H and C were tested on social behavior and food preference [49–51] before beginning the present experiment.

2.2. Neuroimaging and surgical procedures

All procedures were approved by the Committee on Laboratory Animal Welfare of the University of Texas Health Science Center at Houston. MR imaging procedures were performed while the animals were sedated with ketamine/xylazine (7:3 mixture of Ketamine hydrochloride, 100 mg/ml, and Xylazine, 20 mg/ml, i.m.) and their head secured in a non-ferromagnetic stereotaxic apparatus (Crist Instruments Co., Inc., Damascus, MD). Measurements