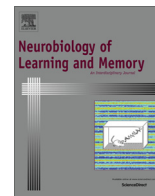




Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

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

Memory consolidation and expression of object recognition are susceptible to retroactive interference



María Eugenia Villar^{a,1}, María Cecilia Martínez^{b,1}, Pamela Lopes da Cunha^a, Fabricio Ballarini^a, Haydee Viola^{a,c,*}

^a Instituto de Biología Celular y Neurociencias “Prof. Eduardo de Robertis”, Facultad de Medicina – Universidad de Buenos Aires – CONICET, Paraguay 2155 – 3rd floor, Ciudad Autónoma de Buenos Aires, C1121ABG Buenos Aires, Argentina

^b Laboratorio de Fisiología de Circuitos Neuronales, Departamento de Fisiología, Facultad de Medicina, Instituto de Fisiología y Biofísica “Bernardo Houssay”, Universidad de Buenos Aires – CONICET, Paraguay 2155 – 7th floor, Ciudad Autónoma de Buenos Aires, C1121ABG Buenos Aires, Argentina

^c Departamento de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Intendente Güiraldes 2160, Ciudad Universitaria, Buenos Aires, Argentina

ARTICLE INFO

Article history:

Received 11 February 2016

Revised 19 April 2016

Accepted 24 April 2016

Available online 27 April 2016

Keywords:

Object recognition task
Retroactive interference
Long-term memory
Dorsal hippocampus
Medial prefrontal cortex
Rat

ABSTRACT

With the aim of analyzing if object recognition long-term memory (OR-LTM) formation is susceptible to retroactive interference (RI), we submitted rats to sequential sample sessions using the same arena but changing the identity of a pair of objects placed in it. Separate groups of animals were tested in the arena in order to evaluate the LTM for these objects. Our results suggest that OR-LTM formation was retroactively interfered within a critical time window by the exploration of a new, but not familiar, object. This RI acted on the consolidation of the object explored in the first sample session because its OR-STM measured 3 h after training was not affected, whereas the OR-LTM measured at 24 h was impaired. This sample session also impaired the expression of OR memory when it took place before the test. Moreover, local inactivation of the dorsal Hippocampus (Hp) or the medial Prefrontal Cortex (mPFC) previous to the exploration of the second pair of objects impaired their consolidation restoring the LTM for the objects explored in the first session. This data suggests that both brain regions are involved in the processing of OR-memory and also that if those regions are engaged in another process before finishing the first consolidation process its LTM will be impaired by RI.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

Recognition is the ability to distinguish the occurrence of a stimulus that was previously presented from one that was not (Squire, Wixted, & Clark, 2007). Animals can form recognition memories about the identity of individual objects and also about their location or recency (Barker, Bird, Alexander, & Warburton, 2007). In this work, we focus on the object recognition (OR) memory, which is based on the animals ability to discriminate a new object from an old one when they are presented in a familiar arena. This task is used to investigate the “what” aspect of episodic-like memories that also include the recall of information about “where

and when” aspects of an event (Dere, Huston, & De Souza Silva, 2005; Ergorul & Eichenbaum, 2004; Tulving, 2002).

A single exploration session episode in an OR task leaves a lasting complex memory trace. As a general mechanism of memories’ formation, after the acquisition of information, the storage of a long-term memory (LTM) trace goes through a consolidation phase. This represents a labile period susceptible to disruption which probably accounts for an adaptive function, enabling those endogenous processes activated by an experience to modulate the strength of the memory (McGaugh, 2000). Quite recently this unstable period of consolidation was suggested to give new memories an opportunity to interact and communicate with others. In that sense, it was shown a correlation between the susceptibility to interference of a memory and learning transfer to the another memory task (Mosha & Robertson, 2015). Regarding this, there are many studies on the effect of retroactive interference (RI), a type of amnesia characterized by the disruptive effect of a new learning experience over previously encoded material (Wixted, 2004). The objective of the present work is to investigate if

* Corresponding author at: Laboratorio de Memoria, Instituto de Biología Celular y Neurociencia “Prof. E. De Robertis”, Facultad de Medicina, Universidad de Buenos Aires – CONICET, Paraguay 2155 3 piso, C1121ABG Buenos Aires, Argentina.

E-mail addresses: maeuvi@yahoo.com (M.E. Villar), ceciliamartinez256@gmail.com (M.C. Martínez), pamelopes@gmail.com (P. Lopes da Cunha), faballarini@gmail.com (F. Ballarini), hviola@fmed.uba.ar (H. Viola).

¹ These authors contributed equally to this work.

OR-LTM formation is susceptible to RI within the consolidation window. Besides we will determine what kind of events are able to interfere with the OR memory and which are the brain regions taking part in this process.

We have recently shown that object-in-context LTM formation is very sensitive to RI elicited by the exploration of a different context (novel or familiar) with different objects (novel or familiar) placed in it. This interference occurs in a restricted temporal window and works on the LTM consolidation phase, leaving intact the short-term memory (STM) expression (Martínez, Villar, Ballarini, & Viola, 2014). However, the memory for the object presented in the first trial is insensitive to the RI elicited by a different object when it is presented in a different context (Martínez et al., 2014). In other words, animals can remember the object but not the context in which it was explored during the training session. Thus, is it the OR memory immune to RI or is it necessary to increase the complexity of the task in order to observe interference on the rat's ability to remember the identity of the object? In order to resolve this issue, here we submitted rats to sequential object exploration sessions in an arena, changing the identity of the objects placed in it.

As it was previously mentioned, the formation of recognition memory includes several features to be encoded: a particular object or person ("what"), the context where the experience took place – which can be the arena itself or a location within the arena ("where") – and the particular time in which the event occurred ("when"). Moreover, recognition memory is widely viewed as consisting of two components: *recollection*, regarding to remembering specific details including the context and/or the particular time in which the experience took place, and *familiarity* which involves simply knowing that an item was presented (Squire et al., 2007; Yonelinas, 2002). There is an ongoing debate about the anatomical substrate of recognition memory. It was proposed that these components are relayed in different brain regions (Brown & Aggleton, 2001; Warburton & Brown, 2015; Winters, 2004), being recollection dependent on the hippocampus and familiarity on the adjacent perirhinal cortex. However, an alternative perspective suggests that these structures work in a cooperative and complementary way and they are both involved in such components, what could be interpreted in terms of strong and weak memories (Clark, 2013; Cohen & Stackman, 2015; Squire et al., 2007). Related to this, the contribution of the perirhinal cortex in OR memory has been well demonstrated (Barker, Bashir, Brown, & Warburton, 2006; Ho et al., 2015; Mendez, Arias, Uceda, & Arias, 2015; Winters & Bussey, 2005); however, the involvement of the hippocampal (Hp) region remains controversial (Barker & Warburton, 2011; Broadbent, Squire, & Clark, 2004; Cohen et al., 2013; Kim, Kim, Lee, Park, & Ryu, 2014; Mumby, Gaskin, Glenn, Schramek, & Lehmann, 2002; Rossato et al., 2007, 2015; Vnek & Rothblat, 1996; Winters, 2004; Zalcman, Federman, de la Fuente, & Romano, 2015). Thus, we explored the participation of the dorsal hippocampus and the medial Prefrontal Cortex (mPFC), another region associated to recognition memory (Barbosa et al., 2013; Morici et al., 2015; Pezze, Marshall, Fone, & Cassaday, 2015), in the formation of LTM for the "what" aspect of this memory.

In sum, our results suggest that OR-LTM formation was retroactively interfered only when a new (but not familiar) object was explored in the same arena within a critical time window related to the consolidation of this memory trace. This type of interfering session also impaired the expression of the OR memory when it occurred before the test session. Moreover, our data suggests that the dorsal Hp and the mPFC are both involved in the processing of OR memory formation, and that if these brain regions are committed in another process before finishing the consolidation of the former, this OR-LTM will be impaired.

2. Materials and methods

2.1. Subjects

Male adult Wistar rats weighing 180–250 g were housed in groups of 5–6 per cage, maintained under a 12-h light/12-h dark cycle (21 °C) with food and water *ad libitum*. They were handled for three min for three consecutive days to reduce emotional stress. All procedures complied with the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publications No. 80-23, revised 1996) and were approved by the Animal Care and Use Committee of the University of Buenos Aires.

2.2. Surgery and drugs

For cannulae implantation rats were deeply anesthetized (70 mg/kg ketamine; 8 mg/kg Xylazine) and 22-G cannulae were stereotaxically aimed to either the CA1 region of the dorsal Hp at coordinates A –3.9 mm, L ±3.0 mm, V 3.0 mm or to the mPFC at coordinates A +3.2 mm, L ±0.75 mm, V –3.2 mm (Paxinos & Watson, 2007, see Fig. 5). All coordinates are relative to the bregma in a flat position with respect to the lambda. Cannulae were fixed to the skull with dental acrylic. Animals received a subdermal application of analgesics and antibiotics at the moment of the surgery (Meloxicam 0.2 mg/kg, gentamicin 3 mg/kg) and were allowed to recover from surgery for four days. Drugs were infused using a 30-G needle with its tip protruding 1.0 mm beyond the guide. The entire bilateral infusion procedure took about 2 min, including 45 s for the infusions themselves, first on one side and then on the other. Cannulae were left in place for 1 additional min to minimize back-flow. Histological examination of cannulae placements was performed after the experiments by the infusion of 0.5 µl of 4% methylene blue in saline solution. Briefly, after the end of the behavioral procedures, methylene blue in saline was infused as indicated above. Animals were killed by decapitation 15 min after and their brains were sliced to check the infusion area (maximum spread of about 1.5 mm³). Only data from animals with correct cannulae implants (95% of the rats) were included in statistical analyses.

The GABA_A agonist muscimol (Sigma, USA) was applied to temporarily inactivate the hippocampal subregion CA1 and the mPFC. The dose infused (0.1 µg of muscimol in 0.5 µl saline solution per side) was reported to be effective (Gonzalez et al., 2013).

2.3. Behavioral training

2.3.1. Habituation

Initial habituation sessions were carried out to familiarize the rats with the apparatus in which training would take place (context). Habituation consisted of one daily session of 12 min in the arena to be used throughout the experimental protocol. Unless indicated to the contrary, all subjects were habituated in two consecutive days to the arena without objects.

2.3.2. Object recognition (OR) task

OR consists of a sample session in which a pair of objects is presented, delay and a test phase where rats explore this object and a novel one. In this paradigm, rats' spontaneous preference for novelty is used to calculate an index of the memory for the object explored in the sample session (Clark & Martin, 2005). As rodents present this innate preference by novel objects, OR task does not require explicit rule learning and also does not require extensive pre-training. They readily approach novel objects and explore them with their vibrissae, nose and forepaws. The percentage of

Download English Version:

<https://daneshyari.com/en/article/5043333>

Download Persian Version:

<https://daneshyari.com/article/5043333>

[Daneshyari.com](https://daneshyari.com)