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Article *in* Nature Neuroscience · May 2007

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Memory consolidation or transformation: context manipulation and hippocampal representations of memory

Gordon Winocur[1–4], Morris Moscovitch[1,3,5] & Melanie Sekeres[6]

The traditional view is that the hippocampus is necessary for retaining memories until they are consolidated in their original form in the neocortex. An alternative view is that the original memory, which is hippocampus- and context-dependent, becomes transformed with time to one that is more schematic and independent of the hippocampus. By manipulating context in two protocols that are widely used to investigate hippocampal-neocortical interactions in memory, we find evidence for the transformation view.

A major challenge facing cognitive scientists is to understand how memories become permanently represented in the brain. The traditional view is that the hippocampus is necessary for retaining context-dependent memories until they are consolidated in their original form in neocortical structures[1,2]. An alternative view argues that, with time, the original memory is transformed from one that is detailed and context-dependent to one that is more schematic and generic, capturing the gist of the original, but shedding much of the context. By this view, it is the transformed memory, not the original one, that is represented in extrahippocampal structures[3–5]. In this study, we provide evidence that supports the transformation view by manipulating context in two animal protocols that are widely used to study hippocampal-neocortical interactions in memory: socially acquired food preference[6–8] and contextual fear conditioning[9–11]. Both accounts predict that making hippocampal lesions before acquisition should eliminate the effects of context at short and long delays. However, they make different predictions about anterograde memory in intact animals. According to the transformation hypothesis, changes in context will affect performance in intact animals shortly after acquisition, when context-dependent memories dominate, but not at longer delays, when gist or schematic versions take over. In contrast, consolidation theory predicts that changes in context should have similar effects at both intervals.

In the food-preference task, a preference is established when a subject rat (S-rat) sniffs the breath of a demonstrator rat (D-rat) that has consumed a sample food with a distinct aroma. When given a choice between the sample and an unfamiliar aromatic food, the S-rat chooses the sample. Rats were tested 1 or 8 d following training, in the same (CXT-S) or a different context (CXT-D). In contextual fear-conditioning, rats are shocked in a test chamber open to the surrounding environment, which provides the context for conditioning. As a result, conditioned fear, in the form of freezing, is exhibited in that context. Memory was assessed at short (1 d) and long (28 d) delays, in the same or a different context. The delays correspond to the beginning and end points of the purported consolidation time in the respective tasks. That is, hippocampal lesions, made within the short delays and before consolidation has occurred, interfere with memory for the food preference[6] or the contextual fear response[9]. At the long delays, when the consolidation process presumably is complete, hippocampal lesions had no effect on memory for either response[6,9]. To confirm that our context manipulations were linked to hippocampal function, rats with hippocampal lesions were tested in the same manner (**Supplementary Methods** online). The study was approved by the Trent University Animal Care Committee and was conducted in accordance with the relevant guidelines.

The lesions typically destroyed about 67% of the hippocampus (**Fig. 1** and **Supplementary Note** online). In both food-preference and contextual fear conditioning, intact rats performed significantly

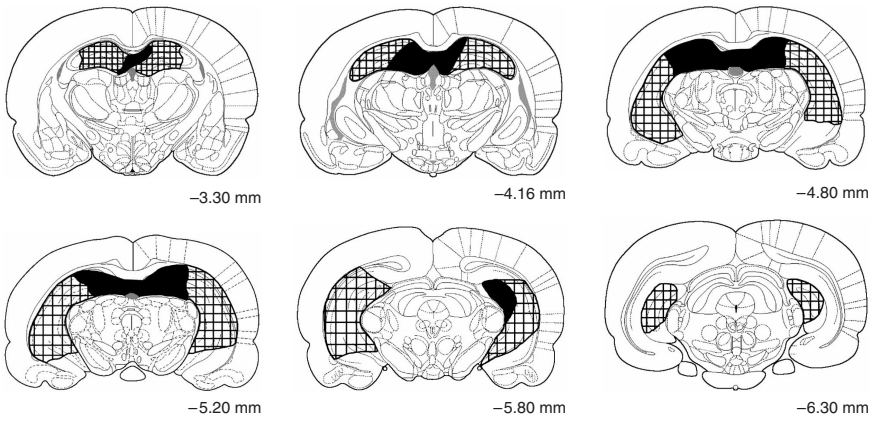

Figure 1 Maximal (grid) and minimal (dark) extents of hippocampal lesions.

[1]Rotman Research Institute, Baycrest Centre, 3560 Bathurst Street, Toronto, Ontario, M6A 2E1, Canada. [2]Department of Psychology, Trent University, 1600 West Bank Drive, Peterborough, Ontario, K9J 7B8, Canada. [3]Department of Psychology, University of Toronto, 100 St. George Street, Toronto, Ontario, M5S 3G3, Canada. [4]Department of Psychiatry, University of Toronto, 250 College Street, Toronto, Ontario, M5T 1R8, Canada. [5]Department of Psychology, Baycrest Centre, 3560 Bathurst Street, Toronto, Ontario, M6A 2E1, Canada. [6]Department of Physiology, University of Toronto, 1 King's College Circle, Toronto, M5S 1A8, Ontario, Canada. Correspondence should be addressed to G.W. (gwinocur@rotman-baycrest.on.ca).

Received 8 January; accepted 23 February; published online 1 April 2007; doi:10.1038/nn1880

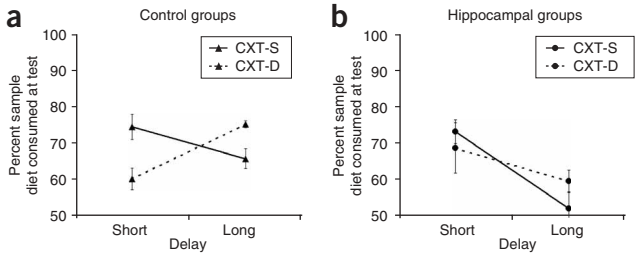

Figure 2 Food preference. Percentage of sample food consumed by (**a**) control and (**b**) hippocampal groups in the food-preference task at 1- or 8-d intervals in CXT-Same or CXT-Different condition. Error bars represent ± s.e.m.

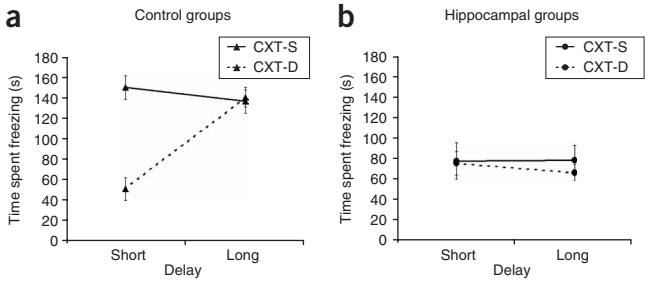

Figure 3 Contextual fear conditioning. Time spent freezing by (**a**) control and (**b**) hippocampal groups in the fear-conditioning task at 1- or 28-d intervals in CXT-Same or CXT-Different condition. Error bars represent ± s.e.m.

better in CXT-S than CXT-D shortly after acquisition (**Figs. 2a** and **3a**, food preference: $t_{18} = 2.89$, $P = 0.010$; contextual fear-conditioning: $t_{13} = 6.17$, $P < 0.001$). At longer delays, and in both tasks, intact rats 'improved' in CXT-D (food preference: $t_{14} = 4.79$, $P = 0.0003$; contextual fear-conditioning: $t_{13} = 6.04$, $P < 0.001$). As a result, the difference between CXT-S and CXT-D was eliminated for control rats at the long delay in contextual fear conditioning. In the food preference task, there was a crossover such that, at the long delay, control rats in the CXT-D condition exhibited a stronger preference for the target food than did controls in the CXT-S condition ($t_{17} = 3.30$, $P = 0.006$). The latter effect may relate to the interplay between context-dependent and context-independent memory in the normal brain (see **Supplementary Note**). By context-independent memory, we refer to memory that does not specify the unique configuration of spatial, temporal and local cues that define the learning experience, but rather to memory that is based on its general characteristics (for example, being transported from colony to test room, placed in a box with a grid floor, etc.; see ref. 5 for an elaboration of this view). In contrast, lesioned rats did not distinguish between the two contexts at both delays in either task (**Figs. 2b** and **3b**; for all comparisons, $P > 0.20$). For contextual fear conditioning, lesioned rats performed poorly in comparison with intact rats at both delays in CXT-S (short: $t_{11} = 3.58$, $P = 0.004$; long: $t_{12} = 3.21$, $P = 0.008$), confirming that the hippocampus is crucial for contextual fear conditioning. In the food-preference task, consistent with previous findings[6,8], there was no difference between lesioned and control rats following the 1-d delay ($t < 1$) in CXT-S. At longer delays, hippocampal lesions caused rats to forget the food preference more quickly ($t_{18} = 2.74$, $P = 0.013$) (see **Supplementary Note** for more detailed analyses of the data).

Notably, changing context had different effects at short and long delays in normal rats on both tasks. At short delays, memory was reinstated in the same, but not the different, context in both tasks, whereas at long delays normal rats performed well regardless of context. The results also demonstrate the standard effects of hippocampal lesions on food-preference and contextual fear conditioning when context does not vary between training and test. Changing context had no effect on hippocampal groups on either task at any delay. Also notable is that these effects were obtained in two tasks that differed in several ways, including the information processed (smell versus shock) and the response (appetitive food preference versus aversive freezing) (for similar results in a runway task, see ref. 12; see also **Supplementary Note**).

The finding that memory was context-sensitive at relatively short delays and that this sensitivity was mediated by the hippocampus is consistent with the view that initially memories are inextricably linked to details of the environment in which they were formed (for example, a specific room with unique cues, spatial configuration, lighting, etc.). With the passage of time, contextual sensitivity is diminished, and the learned response can be elicited by new environments that share general, but not specific, features of the original learning situation (see above). This view of memory transformation helps to explain the counter-intuitive finding that intact rats' performance in the altered contexts appears to improve at the long delays.

The transformation process refers to the increasing dominance of gist over context-specific memory as time goes by; it does not imply that the original, context-dependent memory is necessarily lost. Such memories may continue to be available, along with their gist versions, but the extent to which one or the other influences behavior likely depends on several factors (**Supplementary Note**). In this study, we emphasized the passage of time, but the degree of learning, salience of the context, and emotion are among the other factors that bear investigation.

Our results provide the basis for a framework of how hippocampal-neocortical interactions are modified over time (see **Supplementary Note**). They suggest that the temporal memory gradient seen after hippocampal lesions in retrograde amnesia is not the result of consolidating the identical memory in the neocortex by strengthening connections there. Rather, the gradient reflects the transformation of a memory from a hippocampal-neocortical ensemble that codes the context-dependent features of the event, to an extra-hippocampal, neocortical representation of its general features that are independent of context. Insofar as memory for the specific context is retained, it will continue to depend on the hippocampus no matter how long ago it was acquired (refs. 3,5; see **Supplementary Note**).

Functional neuroimaging and lesion studies in humans provide converging evidence for the transformation hypothesis. Together, they show that (i) all memories initially implicate the hippocampus; (ii) as time passes, only detailed, episodic memories, which correspond to context-dependent memories in animals, continue to do so, whereas (iii) semantic memories, which correspond to context-independent memories, are represented outside of the hippocampus (refs. 4,5,13; but see ref. 14).

In sum, the memory transformation hypothesis provides a new way of viewing the temporal course of hippocampal-neocortical representations of context-dependent (episodic) and context-independent (semantic) memories. It also opens the possibility for describing a dynamic interaction between hippocampus and neocortex in which the

two types of memories can reinforce each other over an extended period of time (ref. 15; see **Supplementary Note**).

Note: Supplementary information is available on the Nature Neuroscience website.

ACKNOWLEDGMENTS

We thank L. Nadel, P. Frankland, M. Fanselow and P. Gisquet-Verrier for having commented on earlier versions of this paper. We thank M. Binns for statistical advice, and M.-È. Couture and N. Chen for providing technical support. This work was supported by Natural Sciences and Engineering Research Council of Canada (NSERC) grants to G.W. and M.M.

COMPETING INTERESTS STATEMENT

The authors declare no competing financial interests.

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