Learning & Memory

Memory for context becomes less specific with time

Brian J. Wiltgen and Alcino J. Silva

References	This article cites 38 articles, 7 of which can be accessed free at: **http://www.learnmem.org/cgi/content/full/14/4/313#References**
Email alerting service	Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article or **click here**

Notes

To subscribe to *Learning & Memory* go to:
http://www.learnmem.org/subscriptions/

Brief Communication

Memory for context becomes less specific with time

Brian J. Wiltgen[1] and Alcino J. Silva

Departments of Neurobiology, Psychology, Psychiatry and the Brain Research Institute, UCLA, Los Angeles, California 90095, USA

Context memories initially require the hippocampus, but over time become independent of this structure. This shift reflects a consolidation process whereby memories are gradually stored in distributed regions of the cortex. The function of this process is thought to be the extraction of statistical regularities and general knowledge from specific experiences. The current study examined this idea in mice by measuring the specificity of context memories during consolidation. In the first experiment, separate groups of animals were trained with a single shock and tested in the training context or a novel environment 1, 14, 28, or 36 d later. We found a systematic increase in generalization over this period. Initially, mice froze more in the training context, but fear of the novel environment grew over time until animals eventually froze an equivalent amount in both contexts. The second experiment demonstrated that the increase in generalization was due to a loss of detailed information about the context and not fear incubation. In this experiment, mice were exposed to the context and then trained with an immediate shock 1 or 36 d later. Animals trained 1 d after exposure acquired robust context fear that did not generalize across environments. In contrast, mice trained 36 d after exposure froze an equivalent amount in the training context and the novel environment. The same profile was observed in H-ras mutants that exhibit enhanced hippocampal plasticity and learning. These results suggest that context memories are specific early after training when they require the hippocampus, and become more general as they are permanently stored in the cortex.

The hippocampus plays a time-limited role in the retrieval of memory. Damage to this structure produces a loss of recently formed memories and leaves intact those acquired in the remote past (Anagnostaras et al. 1999; Squire et al. 2004; Bayley et al. 2005). As memory becomes independent of the hippocampus, it is thought to be permanently stored in distributed regions of the cortex (Squire and Alvarez 1995; Squire et al. 2004; Wiltgen et al. 2004; Frankland and Bontempi 2005). Consistent with this idea, recent animal studies showed activation of cortical sites and a concurrent deactivation of the hippocampus when old memories were retrieved. Pharmacological inactivation of these same cortical regions during retrieval produced a selective remote memory deficit (Bontempi et al. 1999; Frankland et al. 2004a; Maviel et al. 2004).

Contemporary learning models suggest this reorganization of memory systems reflects an important process, the extraction of statistical regularities, and general knowledge from specific experiences (McClelland et al. 1995; O'Reilly and Rudy 2001). According to these models, the hippocampus rapidly encodes detailed memories (i.e., episodes) and then replays them so that the cortex can slowly extract features that are common across experiences (i.e., semantic memories). Consistent with this idea, episodic memory retrieval in humans includes a detailed re-experiencing of the original time and place where the event occurred (i.e., recollection), while semantic memories are remembered simply as facts and are accompanied by a sense of familiarity (Tulving 1985, 1989; Knowlton and Squire 1995). Imaging studies have also shown that memory retrieved via recollection activates the hippocampus, while retrieval based on familiarity does not (Eldridge et al. 2000).

The goal of the current experiments was to determine whether similar processes occur in mice during context fear conditioning, a task that initially requires the hippocampus, and over time, becomes dependent on the cortex (Kim and Fanselow 1992; Anagnostaras et al. 1999; Frankland et al. 2004a). To do

this, we examined changes in the specificity of context fear over time. Based on the models above, we predicted that fear would be specific to the training context early after learning, when it requires the hippocampus. In contrast, as memory becomes dependent on the cortex, it should begin to generalize to other environments. Our first experiment tested this prediction. The second experiment examined whether changes in generalization over time are due to increases in fear (i.e., incubation) or a loss of details for context memory. The last experiment determined whether a reminder treatment could reduce generalization at remote time points and restore the specificity of context fear.

Results

Fear generalization increases over time

Previous studies have suggested that context memories lose details over time (Riccio et al. 1984; MacArdy and Riccio 1995; Houston et al. 1999; Balogh et al. 2002; Biedenkapp et al. 2005; McAllister and McAllister 2006). We confirmed this result in the first experiment. Mice were trained with a single footshock and tested 1, 14, 28, or 36 d later ($n = 26, 29, 30, 30$) in the training context and a novel environment. Figure 1A shows that fear of the training context was stable over time ($F < 1$). In contrast, fear of the novel environment (i.e., generalization) increased over time ($F_{(3,111)} = 4.78$, $P < 0.05$). As a result, mice froze significantly more in the training context than in the novel environment early after training (1 d and 14 d; Fisher's PLSD, $P < 0.05$), but not later (28 d and 36 d; Fisher's PLSD, $P < 0.05$). To illustrate this reduced specificity of context fear over time, we plotted the freezing data at each time point as a discrimination ratio (training context)/(training context + novel environment). A ratio of 1 indicates that mice were able to discriminate the contexts perfectly, and a ratio of 0.5 means that they were unable to discriminate. Figure 1B shows a systematic decrease in the discrimination ratio over time ($F_{(3,111)} = 3.612$, $P < 0.05$). These results suggest that context fear memories are initially specific, but become more general with time.

Many laboratories, including our own, have reported that fear memories sometimes become stronger with the passage of

[1]**Corresponding author.**
E-mail bwiltgen@ucla.edu; fax (310) 794-7088.
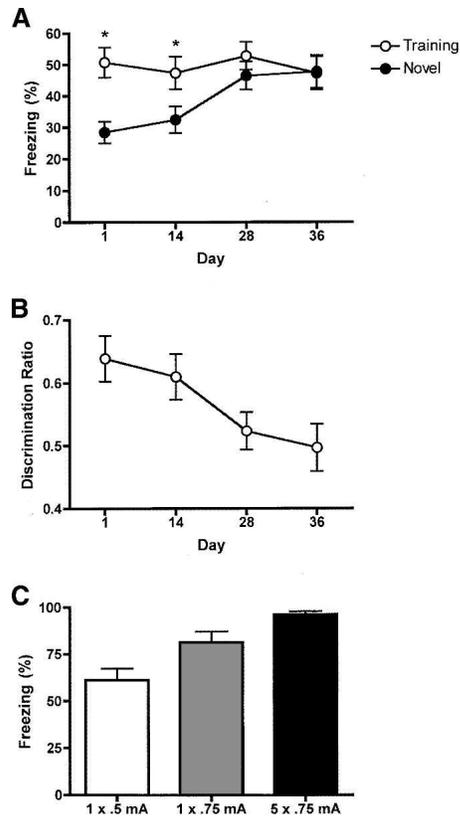Article is online at http://www.learnmem.org/cgi/doi/10.1101/lm.430907.

Figure 1. (*A*) Mean (± SEM) percentage of freezing during tests in the training context and a novel environment. Separate groups of mice were tested 1, 14, 28, and 36 d after training. (*) A statistically significant difference (*P* < 0.05). (*B*) Mean (± SEM) discrimination ratio for each test day calculated from freezing scores in the training context and the novel environment (training/training + novel). (*C*) Mean (± SEM) percentage of freezing in groups of mice receiving a single 0.5 mA shock, a single 0.75 mA shock, or five 0.75 mA shocks, and then tested the next day.

time (Houston et al. 1999; Balogh et al. 2002; Frankland et al. 2004a), a phenomenon called fear incubation (Eysenck 1968). It is possible that fear incubation and not the loss of contextual details is responsible for the increased generalization that we observed in the first experiment. Although fear of the training environment did not incubate in this experiment, animals may have been at a performance ceiling. We tested this by comparing freezing in mice trained with a single 0.5 mA shock (*n* = 15) with those trained with a single 0.75 mA shock (*n* = 8) and those receiving five 0.75 mA shocks (*n* = 8). Animals were tested 1 d later. Figure 1C shows the results of this experiment. Mice that received one or five 0.75 mA shocks froze significantly more than those receiving a single 0.5 mA shock (Fisher's PLSD, *P* < 0.05). This suggests that the lack of fear incubation in our training environment was not simply due to a performance ceiling.

Memory for context becomes less specific over time

If increased generalization results from context memories becoming less specific with time, then we should be able to observe the same phenomenon in the absence of fear. To test this idea, we used context pre-exposure and immediate shock training (Fanselow 1990; Rudy and O'Reilly 2001). It is well established that rats and mice need a minimum amount of time in the training environment to learn about the context. Delivering shock immediately after placement in the context produces no learning, a deficit that can be overcome by pre-exposing the animals

to the environment (Fanselow 1990; Wiltgen et al. 2001; Frankland et al. 2004b). Pre-exposure rescues learning because it allows animals to form a representation of the context, which they can readily recall during the subsequent training session (Rudy and O'Reilly 1999). Therefore, we used the pre-exposure procedure to probe the specificity of context memory over time. Mice were first pre-exposed to the training context for 10 min. A group of control animals was transported to the holding room, but not removed from their homecages. Separate groups of mice were then trained with an immediate shock in the training context 1 or 36 d later. Over the next 2 days, they were tested in both the training context and a novel environment.

Figure 2A shows the results of this experiment. First, as expected, nonexposed animals (*n* = 9) froze significantly less in the training context than exposed animals (*n* = 15) ($F_{(1,22)}$ = 50.25, *P* < 0.05). In addition, context fear in exposed animals that were trained 1 d later (Recent) was specific to the training context. These animals froze significantly more in the training context than in the novel environment ($F_{(1,14)}$ = 51.834, *P* < 0.05). Mice that were trained 36 d after pre-exposure (Remote; *n* = 13) also froze more than mice that were not exposed ($F_{(1,20)}$ = 9.75, *P* < 0.05), but their fear was not specific to the training context. They froze an equivalent amount in the training context and the novel environment (*F* < 1). Since the training-to-test interval was equivalent for the Recent and Remote groups in this experiment, fear incubation cannot be used to explain these results. Instead, consistent with our interpretation of the first experiment,
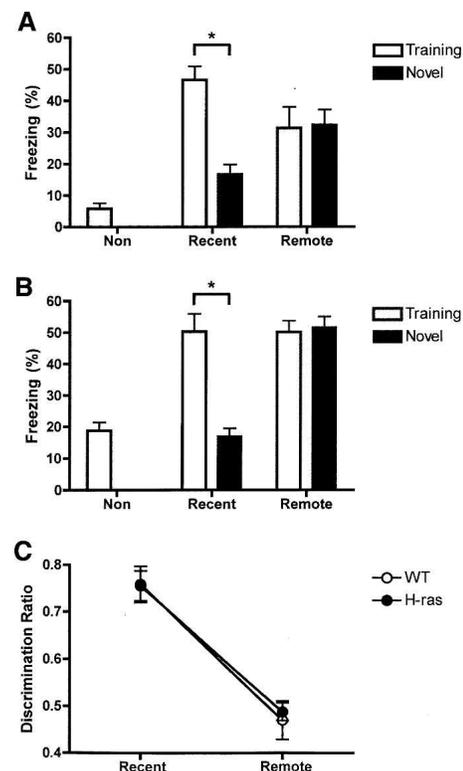

Figure 2. (*A*) Mean (± SEM) percentage of freezing during tests in the training context and a novel environment. Some mice were not exposed to the training context before immediate shock training (Non), some were exposed 1 d before training (Recent), and others were exposed 36 d before training (Remote). (*) A statistically significant difference (*P* < 0.05). (*B*) Mean (± SEM) percentage of freezing in H-ras mutants during tests in the training context and a novel environment. Training conditions were the same as above. (*) A statistically significant difference (*P* < 0.05). (*C*) Mean (± SEM) discrimination ratio for WT and H-ras mice during the recent and remote context tests.

memory for the context appears to change across time. When mice are asked to recall previously learned context memories after a long interval has passed, they remember only basic information that generalizes to other environments.

We next determined whether the generalization process is affected by increases in hippocampal plasticity. To do this, we trained mice that express a constitutively active form of H-ras (G12V) in the forebrain using the behavioral procedures just described. Our lab recently showed that this mutation enhances hippocampal long-term potentiation (LTP) and learning (Kushner et al. 2005). Increasing plasticity in the hippocampus could produce a more specific memory that does not generalize at remote time points. Alternatively, the loss of memory specificity could be a process that is independent of hippocampal plasticity mechanisms. As seen in Figure 2B, animals exposed to the context and trained 1 d later (Recent; $n = 15$) showed enhanced conditioning compared with nonexposed mice (Non; $n = 6$) ($F_{(1,19)} = 7.67$, $P < 0.05$) and this learning was specific to the training context ($F_{(1,14)} = 50.63$, $P < 0.05$). Context memories also became less specific as the interval between pre-exposure and training was increased. Mice trained 36 d after exposure (Remote; $n = 21$) froze an equivalent amount in the training context and the novel environment ($F < 1$). Therefore, just like in wild-type mice, context memories in H-ras mutants become less specific with the passage of time. This is illustrated in Figure 2C, which plots changes in the discrimination ratio at the recent and remote time points. There was a significant decrease in the discrimination ratio across time ($F_{(1,60)} = 76.59$, $P < 0.05$) that was equivalent for wild-type and mutant animals ($F < 1$). This result suggests that increasing hippocampal plasticity does not necessarily prevent the loss of memory specificity over time.

A reminder treatment restores context discrimination

The first two experiments demonstrate that context memories become more general with time. This finding could be interpreted in at least two ways. The original, detailed memory for context could be transformed into a generalized representation and integrated into existing knowledge structures by the cortex (e.g., semantic memory) (McClelland et al. 1995; O'Reilly and Rudy 2001). Alternatively, the original memory could remain intact and simply become difficult to retrieve at remote time points due to forgetting (Bouton et al. 1999). The current experiment tested between these alternatives by using a reminder treatment. Some mice ($n = 20$) were re-exposed to the original training context for 1 min (Reminder) 35 d after training, while others ($n = 21$) remained in their home cage (No reminder). The following day, half of the animals from each group were tested in the training context (Reminder, $n = 9$, No reminder, $n = 10$) and the other half in the novel environment (Reminder, $n = 11$, No reminder, $n = 11$). If mice have difficulty retrieving a detailed memory of the environment then a reminder session should help them retrieve this representation and reduce generalization. In contrast, if the original memory has been transformed into a new generalized representation, then the reminder treatment should have little effect.

The results are presented in Figure 3. Consistent with our first experiment, mice that were not reminded of the training context generalized to the novel environment. They froze an equivalent amount in both contexts ($F < 1$). In contrast, mice that received the reminder treatment were able to discriminate, and froze more in the training context than in the novel environment ($F_{(1,18)} = 5.45$, $P < 0.05$). This result suggests that increased generalization at remote time points is due, at least in part, to the forgetting of specific features of the context. The original detailed context memory does not appear to be lost over
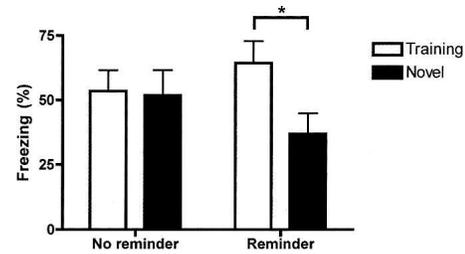

Figure 3. (A) Mean ($\pm$ SEM) percentage of freezing during tests in the training context and a novel environment. Some mice received a 1-min reminder treatment before the test (Reminder) and others did not (No reminder). (*) A statistically significant difference ($P < 0.05$).

time, a finding that is consistent with previous studies on forgetting (Zhou and Riccio 1994, 1996; Rosas and Bouton 1997).

Discussion

The current results illustrate that memory for context is specific shortly after learning and becomes more general with the passage of time. Mice were able to discriminate between the training context and a novel environment 1 and 14 d after conditioning, a period of time when context fear is known to depend on the hippocampus (Kim and Fanselow 1992; Maren et al. 1997). Context fear became less specific and generalized to a novel environment 28 and 36 d after training, time points when the cortex is important for retrieval (Frankland et al. 2004a). These results suggest that context generalization may be a useful index of the consolidation process.

Previous studies have also suggested that context memories become less specific with time (Riccio et al. 1984; MacArdy and Riccio 1995; Bouton et al. 1999; Houston et al. 1999; Balogh et al. 2002; Biedenkapp et al. 2005; McAllister and McAllister 2006). The current results are consistent with these findings and demonstrate that increases in context generalization are not simply the result of fear incubation. Two pieces of evidence support this conclusion. First, we observed increases in fear over time only in the novel environment. This selectivity was not due to a performance ceiling in the training context, as mice given more intense training procedures were able to exhibit more fear. Second, we found similar increases in generalization following context exposure alone (i.e., in the absence of shock). Mice pre-exposed to the context and then trained with an immediate shock 36 d later showed robust generalization to a novel environment. The same amount of generalization was not observed in mice trained 1 d after pre-exposure. Nonetheless, fear incubation has been observed in many laboratories, including our own (Houston et al. 1999; Balogh et al. 2002; Frankland et al. 2004a). This suggests that two distinct processes can occur following context fear conditioning: a loss of contextual details and a general increase in fear. It is likely that both contribute to the magnitude of fear generalization over time.

The fact that context memory becomes less specific with time fits nicely with contemporary models of consolidation (McClelland et al. 1995; O'Reilly and Rudy 2001; Nadel et al., in press). According to these models, the function of the consolidation process is the extraction of general information from specific experiences. The hippocampus encodes detailed information about recent events and then replays them so that the cortex can gradually extract generalities. These models predict that as context memories become independent of the hippocampus and are stored in the cortex, they should lose details and become more general in nature. The current experiments confirmed this prediction.

We also found that a reminder treatment could be used to

restore the specificity of context fear at remote time points. This is an interesting result, because it implies that the original context memory remains intact and can be retrieved under certain conditions. Previous studies on forgetting have found similar effects (Zhou and Riccio 1994, 1996; Rosas and Bouton 1997). This has important implications for theories of consolidation, because some models argue that as memory is transformed into a more general form, the original detailed information is lost (for a detailed discussion of these issues, see Nadel et al., in press). Instead, our data suggest that animals are able to retrieve either a specific or generalized memory of context at remote timepoints, depending on the conditions. This finding may be related to recent studies on reconsolidation, showing that short reminders given months after training can make context fear once again dependent on the hippocampus (Debiec et al. 2002). Together, these data imply that after a period of time animals recall a generalized memory of context that is stored outside of the hippocampus, but remain capable of accessing the original detailed event via the hippocampus if they are reminded of it. If true, this finding is at odds with consolidation models that predict a loss of hippocampal information as cortical memory traces are formed (McClelland et al. 1995; Nadel et al., in press).

Our experiments also determined whether generalization is affected by changes in hippocampal plasticity. This was accomplished by examining mice that express an active form of H-ras (G12V) that enhances both hippocampal LTP and learning (Kushner et al. 2005). Just like wild-type mice, these animals showed increases in generalization over time. This finding suggests that generalization of context memory may occur through a process that is independent of hippocampal plasticity. Instead, it may involve changes in cortical plasticity like those observed in the medial prefrontal cortex following fear conditioning (Frankland et al. 2004a). However, it is important to note that enhanced plasticity in our H-ras mutants may not be specific to the hippocampus, as the transgene is expressed throughout the forebrain.

The human hippocampus is also important for the acquisition and retrieval of detailed memory representations (Rosenbaum et al. 2001; Moscovitch et al. 2006). For example, the hippocampus is activated when people remember events by recollecting details about them, but not when similar events are recognized based on a feeling of familiarity (Eldridge et al. 2000). Interestingly, studies have shown that recollection decays more quickly than familiarity over long intervals. As a result, many items that are initially remembered via a recollective process are later recognized by familiarity (Gardiner and Java 1991; Knowlton and Squire 1995; Tunney and Bezzina 2006). A similar phenomenon could be responsible for our current results. Recently formed context memories may be retrieved via a recollection-like process that involves the hippocampus, while remote context memories are retrieved through a familiarity-like process that involves regions of the cortex. Future studies can examine this hypothesis using the current behavioral procedures, which we believe provide a useful way to study changes in memory and its retrieval over time.

Materials and Methods

Subjects

In the first and third experiment, F_1 hybrids were generated by breeding C57BL/6 (Taconic) males and 129SvE (Jackson) females. In the second experiment, mice were generated by breeding male animals positive for H-ras (maintained in the C57BL/6 background) with 129SvE females. These mice were genotyped as previously described (Kushner et al. 2005). All mice ranged from 3 to 6 mo of age and were group housed with free access to food and

tap water. They were maintained on a 12:12 h light:dark cycle in the Herbert L. Washington Vivarium in the Department of Psychology at UCLA. All experiments were performed during the light phase of the cycle.

Fear conditioning

The apparatus and procedures used in these experiments have been described previously (Anagnostaras et al. 2000). In the first experiment, mice were placed in the conditioning context for 2 min and then a single footshock (2 sec, 0.5 mA) was delivered. One minute after the shock, the mice were removed and returned to their home cage. Animals were tested for 5 min in the training context or a novel environment 1, 14, 28, or 36 d later. The following day they were tested in the opposite environment. The order of these tests was counterbalanced for each time point. The novel environment was structurally different from the training context and had a Plexiglas floor (28×21 cm) and two white plastic sidewalls (24×21 cm) placed at 60° to the floor, forming a triangular enclosure. It was also housed in a room that was dimly lit by a red light bulb. Ninety-five percent ethyl alcohol was used to clean both the training context and the novel environment, and background noise (65 dB) was supplied in both rooms by a HEPA air cleaner (Honeywell Inc.). For the performance control experiment, naïve mice received 1 or 5 footshocks (2 sec, 0.75 mA) in the training environment. In the latter group, the shocks were separated by a 1-min interval. Animals were tested 1 d later in the same environment. These data were compared with those from mice in the first experiment that received a single 0.5-mA shock, and were tested in the training context the following day.

In the second experiment, mice were first exposed to the training context for 10 min (no shock was delivered) or transported to the holding room and left in their home cage as previously described (Wiltgen et al. 2001; Frankland et al. 2004b). One or 36 d later they were placed into the training context, and 5 sec later received a single footshock (2 sec, 0.75 mA). The animals were removed from the context 30 sec after shock and returned to their home cage. The mice were tested over the next 2 d in the training context and a novel environment as described above.

In the third experiment, mice were trained and tested using the same procedures as in the first experiment. In addition, 35 d after training, half of the animals were exposed to the original training environment for 1 min. The remaining mice stayed in their home cage during this period. The following day, half of the reminded and nonreminded mice were tested in the training context and the other half in the novel environment for 5 min.

Acknowledgments

References

Anagnostaras, S.G., Maren, S., and Fanselow, M.S. 1999. Temporally graded retrograde amnesia of contextual fear after hippocampal damage in rats: Within-subjects examination. *J. Neurosci.* **19:** 1106–1114.

Anagnostaras, S.G., Josselyn, S.A., Frankland, P.W., and Silva, A.J. 2000. Computer-assisted behavioral assessment of Pavlovian fear conditioning in mice. *Learn. Mem.* **7:** 58–72.

Balogh, S.A., Radcliffe, R.A., Logue, S.F., and Wehner, J.M. 2002. Contextual and cued fear conditioning in C57BL/6J and DBA/2J mice: Context discrimination and the effects of retention interval. *Behav. Neurosci.* **116:** 947–957.

Bayley, P.J., Gold, J.J., Hopkins, R.O., and Squire, L.R. 2005. The neuroanatomy of remote memory. *Neuron* **46:** 799–810.

Biedenkapp, J., Lopez, D., Sprunger, D., and Rudy, J. 2005. Generalization test reveals rapid forgetting of a hippocampus-dependent contextual-fear memory. In *SFN.* Washington, D.C.

Bontempi, B., Laurent-Demir, C., Destrade, C., and Jaffard, R. 1999.

Time-dependent reorganization of brain circuitry underlying long-term memory storage. *Nature* **400:** 671–675.

Bouton, M.E., Nelson, J.B., and Rosas, J.M. 1999. Stimulus generalization, context change, and forgetting. *Psychol. Bull.* **125:** 171–186.

Debiec, J., LeDoux, J.E., and Nader, K. 2002. Cellular and systems reconsolidation in the hippocampus. *Neuron* **36:** 527–538.

Eldridge, L.L., Knowlton, B.J., Furmanski, C.S., Bookheimer, S.Y., and Engel, S.A. 2000. Remembering episodes: A selective role for the hippocampus during retrieval. *Nat. Neurosci.* **3:** 1149–1152.

Eysenck, H.J. 1968. A theory of the incubation of anxiety-fear responses. *Behav. Res. Ther.* **6:** 309–321.

Fanselow, M.S. 1990. Factors governing one-trial contextual conditioning. *Anim. Learn. Behav.* **18:** 264–270.

Frankland, P.W. and Bontempi, B. 2005. The organization of recent and remote memories. *Nat. Rev. Neurosci.* **6:** 119–130.

Frankland, P.W., Bontempi, B., Talton, L.E., Kaczmarek, L., and Silva, A.J. 2004a. The involvement of the anterior cingulate cortex in remote contextual fear memory. *Science* **304:** 881–883.

Frankland, P.W., Josselyn, S.A., Anagnostaras, S.G., Kogan, J.H., Takahashi, E., and Silva, A.J. 2004b. Consolidation of CS and US representations in associative fear conditioning. *Hippocampus* **14:** 557–569.

Gardiner, J.M. and Java, R.I. 1991. Forgetting in recognition memory with and without recollective experience. *Mem. Cognit.* **19:** 617–623.

Houston, F.P., Stevenson, G.D., McNaughton, B.L., and Barnes, C.A. 1999. Effects of age on the generalization and incubation of memory in the F344 rat. *Learn. Mem.* **6:** 111–119.

Kim, J.J. and Fanselow, M.S. 1992. Modality-specific retrograde amnesia of fear. *Science* **256:** 675–677.

Knowlton, B.J. and Squire, L.R. 1995. Remembering and knowing: Two different expressions of declarative memory. *J. Exp. Psychol. Learn. Mem. Cogn.* **21:** 699–710.

Kushner, S.A., Elgersma, Y., Murphy, G.G., Jaarsma, D., van Woerden, G.M., Hojjati, M.R., Cui, Y., LeBoutillier, J.C., Marrone, D.F., Choi, E.S., et al. 2005. Modulation of presynaptic plasticity and learning by the H-ras/extracellular signal-regulated kinase/synapsin I signaling pathway. *J. Neurosci.* **25:** 9721–9734.

MacArdy, E.A. and Riccio, D.C. 1995. Time-dependent changes in the effectiveness of a non-contingent footshock reminder. *Learn. Motiv.* **26:** 29–42.

Maren, S., Aharonov, G., and Fanselow, M.S. 1997. Neurotoxic lesions of the dorsal hippocampus and Pavlovian fear conditioning in rats. *Behav. Brain Res.* **88:** 261–274.

Maviel, T., Durkin, T.P., Menzaghi, F., and Bontempi, B. 2004. Sites of neocortical reorganization critical for remote spatial memory. *Science* **305:** 96–99.

McAllister, W.R. and McAllister, D.E. 2006. Recovery of conditioned fear by a single postextinction shock: Effect of similarity of shock contexts and of time following extinction. *Learn. Behav.* **34:** 44–49.

McClelland, J.L., McNaughton, B.L., and O'Reilly, R.C. 1995. Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* **102:** 419–457.

Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A., and Rosenbaum, R.S. 2006. The cognitive neuroscience of remote episodic, semantic and spatial memory. *Curr. Opin. Neurobiol.* **16:** 179–190.

Nadel, L., Winocur, G., Ryan, L., and Moscovitch, M. Systems consolidation and the hippocampus: Two views. *Debates Neurosci.* (in press).

O'Reilly, R.C. and Rudy, J.W. 2001. Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychol. Rev.* **108:** 311–345.

Riccio, D.C., Richardson, R., and Ebner, D.L. 1984. Memory retrieval deficits based upon altered contextual cues: A paradox. *Psychol. Bull.* **96:** 152–165.

Rosas, J.M. and Bouton, M.E. 1997. Additivity of the effects of retention interval and context change on latent inhibition: Toward resolution of the context forgetting paradox. *J. Exp. Psychol. Anim. Behav. Process.* **23:** 283–294.

Rosenbaum, R.S., Winocur, G., and Moscovitch, M. 2001. New views on old memories: Re-evaluating the role of the hippocampal complex. *Behav. Brain Res.* **127:** 183–197.

Rudy, J.W. and O'Reilly, R.C. 1999. Contextual fear conditioning, conjunctive representations, pattern completion, and the hippocampus. *Behav. Neurosci.* **113:** 867–880.

Rudy, J.W. and O'Reilly, R.C. 2001. Conjunctive representations, the hippocampus, and contextual fear conditioning. *Cogn. Affect. Behav. Neurosci.* **1:** 66–82.

Squire, L.R. and Alvarez, P. 1995. Retrograde amnesia and memory consolidation: A neurobiological perspective. *Curr. Opin. Neurobiol.* **5:** 169–177.

Squire, L.R., Stark, C.E., and Clark, R.E. 2004. The medial temporal lobe. *Annu. Rev. Neurosci.* **27:** 279–306.

Tulving, E. 1985. Memory and consciousness. *Can. Psychol.* **26:** 1–12.

Tulving, E. 1989. Remembering and knowing the past. *Am. Sci.* **77:** 361–367.

Tunney, R.J. and Bezzina, G. 2006. Effects of retention intervals on receiver operating characteristics in artificial grammar learning. *Acta Psychol.* doi:10.1016/j.actpsy.2006.06.002.

Wiltgen, B.J., Sanders, M.J., Behne, N.S., and Fanselow, M.S. 2001. Sex differences, context preexposure, and the immediate shock deficit in Pavlovian context conditioning with mice. *Behav. Neurosci.* **115:** 26–32.

Wiltgen, B.J., Brown, R.A., Talton, L.E., and Silva, A.J. 2004. New circuits for old memories; the role of the neocortex in consolidation. *Neuron* **44:** 101–108.

Zhou, Y. and Riccio, D.C. 1996. Manipulation of components of context: The context shift effect and forgetting of stimulus attributes. *Learn. Motiv.* **27:** 400–407.

Zhou, Y.L. and Riccio, D.C. 1994. Pretest cuing can alleviate the forgetting of contextual stimulus attributes. *Learn. Motiv.* **25:** 233–244.