

Memory's Penumbra: Episodic Memory Decisions Induce Lingerin Mnemonic Biases

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How do we decide if the people we meet and the things we see are familiar or new? If something is new, we need to encode it as a memory distinct from already stored episodes, using a process known as pattern separation. If familiar, it can be used to reactivate a previously stored memory, by a process known as pattern completion. To orchestrate these conflicting processes, current models propose that the episodic memory system uses environmental cues to establish processing biases that favor either pattern separation during encoding or pattern completion during retrieval. To assess this theory, we measured how people's memory formation and decisions are influenced by their recent engagement in episodic encoding and retrieval. We found that the recent encoding of novel objects improved subsequent identification of subtle changes, a task thought to rely on pattern separation. Conversely, recent retrieval of old objects increased the subsequent integration of stored information into new memories, a process thought to rely on pattern completion. These experiments provide behavioral evidence that episodic encoding and retrieval evoke lingering biases that influence subsequent mnemonic processing.

When you walk into a café for the first time, your memory system can both encode the details of this new environment and allow you to remember a similar one where you recently dined with a friend. The often effortless way in which we can encode the present and remember the past belies the complexity of the underlying processes, however. Though decades of theoretical and empirical research (1–5) have improved our understanding of both the neural systems and the computations that underlie episodic memory, the convergence of these lines of research reveals a paradox: Neuroscience research shows that both encoding new memories and retrieving old ones depend on the same specific brain region, the hippocampus (6–8), but computational models propose that encoding and retrieval are differentially supported by computationally incompatible network processes (9). Specifically, episodic encoding is thought to rely on pattern separation, a process that makes overlapping representations more distinct, whereas retrieval is thought to depend on pattern completion, a process that increases overlap by reactivating related memory traces. Because a process that emphasizes overlap cannot simultaneously operate on the same representation as one that deemphasizes it, a potential resolution to the paradox is that the hippocampus can establish processing biases that favor either pattern separation or completion, depending on the current context. This suggests that your likelihood of remembering your earlier lunch with a friend may be biased by the specific hippocampal processing

you were engaged in, even before walking into the café. In fact, neurocomputational models have long hypothesized that neuromodulatory systems may dynamically bias hippocampal processing toward either pattern completion or separation (10–13). Here, we test a prediction derived from these models and provide empirical support for these biases in human behavior.

The crux of our approach lies in the relatively slow action of neuromodulators in the hippo-

campus (14). If switching between pattern completion and separation biases is, in fact, mediated by hippocampal neuromodulatory input, it follows that a processing bias should linger in time and, thus, influence subsequent mnemonic processing. To test this, we presented participants with pictures of novel and familiar objects and asked them to make old/new recognition decisions (see supplementary materials and methods). According to models (10–13), detecting novelty should bias the memory system toward pattern separation to support distinctive encoding of the new information, whereas recognizing that a stimulus was previously experienced should induce a pattern completion bias that supports retrieval of stored representations. We measured lingering biases by presenting participants with critical test trials immediately after unrelated old and new memory decisions. We designed test trials across three different experiments to measure biases both at the time of retrieval decisions and during periods of encoding.

In the first two experiments, we measured biases in retrieval decisions with the use of a modified continuous recognition paradigm that has previously been applied to study pattern separation in the human hippocampus (15, 16). Participants were presented with a series of objects that fell into three categories: novel objects, repeated objects, or objects that were similar but not identical to previously presented ones. Participants were then asked to identify each as new (first presentation), old (exact repetition), or similar (not exact repetition) (Fig. 1A, see

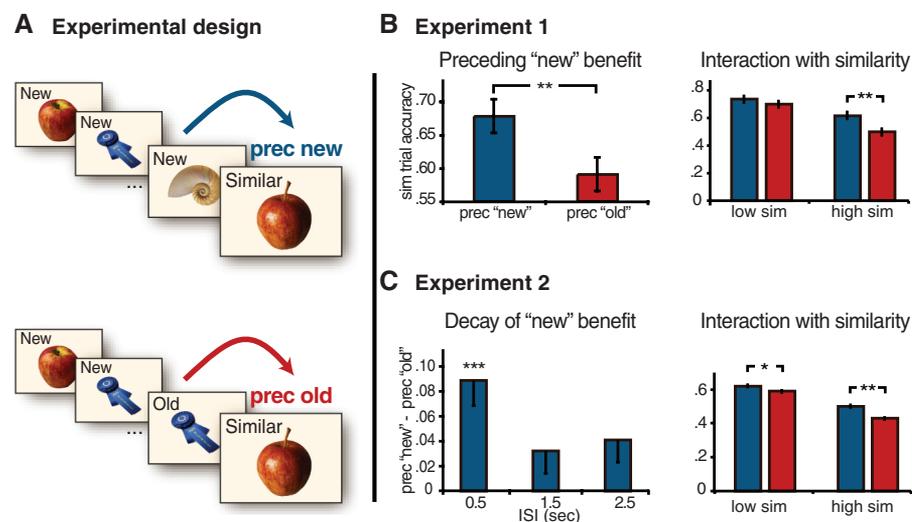


Fig. 1. (A) Participants were presented with a series of objects and asked to identify whether each item is new (first presentation), old (exact repetition), or similar (a modified object). The top sequence provides a preceding new example: The similar object follows a new object. The bottom sequence provides a preceding old example: The similar object follows an old object. (B) Results from experiment 1. (Left) Plot of accuracy on similar trials as a function of the preceding response (new in blue and old in red) ($n = 15$ participants). (Right) The bars on this graph are further divided according to perceptual similarity ratings. (C) Results from experiment 2. (Left) Graph displaying the preceding new benefit (preceding new – preceding old) for similar trial accuracy at an ISI of 0.5, 1.5, and 2.5 s ($N = 52$). (Right) Plot of similarity rating interaction for experiment 2 in the same way as presented above. Error bars mark the standard error of the difference between preceding new and old conditions. * $P < 0.05$, ** $P < 0.005$, *** $P < 0.001$.

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supplementary materials for more task details). Similar trials served as our critical test trials to measure pattern separation/completion biases. Specifically, although participants ($n = 15$) were instructed to respond “similar” to similar objects, the differences were often quite subtle, so similar objects were sometimes mistakenly identified as “old.” Thus, we reasoned that if the memory system was already biased toward pattern completion, these similar stimuli would more often be incorrectly identified as old, whereas if the system was biased toward pattern separation, the likelihood of noticing the small differences would be increased. Hence, we looked for evidence for lingering biases in memory decisions by examining whether participants were more likely to correctly identify similar trials as similar if they followed new trials rather than if they were presented after old trials.

Consistent with our hypotheses, we found that similar trials were more accurately identified as being similar when they were preceded by new trials than when they were preceded by old ones [prec. new = 67.7%, prec. old = 61.7%, $t(14) = 3.41$, $P < 0.005$]. This performance benefit (6%) was even larger (9%) when we binned similar trials based on the preceding response (for example, when participants reported a stimulus as new) rather than the preceding trial type (when a stimulus was actually new) [prec. new = 68.0%, prec. old = 59.4%, $t(14) = 3.32$, $P < 0.005$] (Fig. 1B), suggesting that the critical factor is the subjective memory decision rather than the stimulus type. Moreover, the preceding response still explained a significant portion of the variance in similar trial accuracy after adjusting for several covariates, including preceding trial type, preceding accuracy, and preceding response times (RTs) (Wald $\chi^2 = 8.9$, $P < 0.005$; see supplementary materials for full details and additional control analyses). There was also a similar but nonsignificant trend for the preceding response’s influence on RTs, with similar trials being correctly identified faster when they were preceded by new as compared with old responses [prec. new = 967 ms, prec. old = 988 ms, $t(14) = 2.01$, $P = 0.06$]. Finally, we predicted that similar trials that were difficult, with mnemonic evidence lying close to the decision boundary, would be more influenced by mnemonic biases than similar trials that were easier. We tested this hypothesis by dividing similar trials based on perceptual similarity ratings (see experiment 1a in the supplementary materials). A repeated-measures analysis of variance revealed a significant interaction between the preceding response (old versus new) and similarity rating (high versus low) ($F_{1,28} = 5.27$, $P < 0.05$) (Fig. 1B, also see fig. S4 for a parametric analysis). Consistent with our hypothesis, this interaction was driven by the fact that the preceding response’s influence was largest for the more difficult similar trials, those that were rated as being more similar [high similarity: $t(14) = 3.65$, $P < 0.005$; low similarity: $t(14) = 1.08$, $P = 0.30$].

Experiment 1 demonstrated that memory decisions can influence subsequent ones in a manner consistent with computational models of the hippocampus (10–13). If this bias is, in fact, mediated by neuromodulator action, we reasoned that it should also be temporally limited on the scale of seconds (12, 14). In experiment 2, we measured the time window over which these carry-over effects exert themselves by varying the interstimulus time interval (ISI) that elapsed between trials (0.5, 1.5, and 2.5 s) with a new set of participants ($n = 52$). We replicated the main effect of the preceding response (old versus new) ($F_{1,50} = 21.1$, $P < 0.001$) and the interaction between similarity rating and preceding response ($F_{1,50} = 4.41$, $P < 0.05$). Critically, we also found that the preceding new benefit was time-dependent. Specifically, there was a significant interaction between ISI and preceding response ($F_{2,100} = 3.2$, $P < 0.05$), with the largest preceding-response effect on trial accuracy found for similar trials that were preceded by the shortest ISI [prec. new = 58.3%, prec. old = 49.4%, $t(51) = 4.3$, $P < 0.001$; preceding old versus new differences at longer ISIs were not sig-

nificant] (Fig. 1C). A similar interaction was also found in RTs ($F_{2,100} = 4.2$, $P < 0.05$) (fig. S5B).

In experiment 3, we tested whether old and new memory decisions can also influence subsequent memory formation (Fig. 2, see fig. S6 for example trials). To this end, we modified a paradigm that was designed to assess whether related associations are integrated into newly formed memory traces (17, 18), a process that should be influenced by pattern completion/separation biases. We reasoned that the memory system would be more likely to reactivate previously encountered, but related information after old recognition decisions compared with new decisions and that this reactivation should, in turn, lead to greater integration of the reactivated representations into newly formed memories. To test this hypothesis, we had a new group of participants ($n = 22$) alternate between making old/new object-recognition decisions and encoding overlapping face-scene associations. Critically, these face-scene pairs (A-Y pairs) were associatively related to other face-scene pairs (A-X and B-X pairs) that were learned in an earlier phase of the experiment. Previous research has

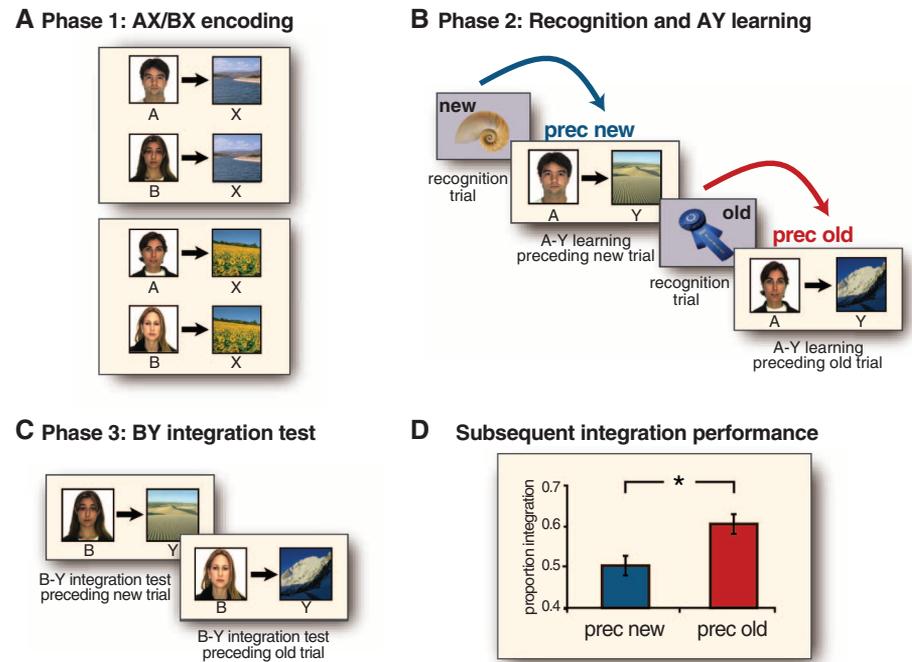


Fig. 2. We used a multiphase design to test integrative encoding. (A) Participants first learned face-scene associations in which pairs of faces were associated with the same scene (A-X and B-X associations). (B) Participants then learned a new scene association for one face from each pair (A-Y association). These A-Y learning trials were interleaved with object-recognition trials. Each A-Y association was preceded by either a novel object (preceding new condition) or one that had been studied at the beginning of the session (preceding old condition). Participants indicated whether each object was old or new. (C) The final phase evaluated whether participants integrated the overlapping associations from the earlier two phases by testing whether they chose to pair the indirectly related faces and scenes (B-Y association). (D) Influence of preceding memory decisions on integration in experiment 3. The graph compares how often participants paired indirectly associated faces and scenes (B-Y associations) during the final test phase. Trials are divided according to whether their learned counterpart (A-Y) was encoded after new (blue) or old (red) objects during the earlier phase. Error bars mark the standard error of the difference between preceding new and old conditions. * $P < 0.05$.

demonstrated that participants tend to integrate these related A-X and B-X pairs into their learning of new A-Y pairs, forming a link between the indirectly associated B and Y stimuli (17–19). To assess the strength of this integration, we subsequently tested how often participants chose to pair faces and scenes that were only indirectly related across the two sets (B-Y pairs). Consistent with our hypothesis, participants were 10% more likely to subsequently show this kind of integration when they encoded the A-Y pairs following old objects as compared with new ones [prec. new = 60.1%, prec. old = 50.1%, $t(21) = 2.1$, $P < 0.05$] (Fig. 2D). Moreover, when participants chose to pair indirectly related stimuli, they did so 71 ms faster if the stimuli had previously been learned after old objects as compared with new ones [prec. new = 1487 ms, prec. old = 1558 ms, $t(21) = 2.2$, $P < 0.05$], again consistent with the interpretation that retrieval improves subsequent integrative encoding.

Together, these results provide behavioral evidence that episodic encoding and retrieval can evoke biases that influence subsequent mnemonic processing, a phenomenon that computational models predict to be the consequence of a tension between episodic encoding and retrieval operations. Importantly, the evidence presented here goes beyond simply demonstrating competition between concurrent encoding and retrieval (20, 21), an effect that could be explained by a bottleneck at various cognitive stages (22); rather, we provide evidence that memory decisions can exert a temporally extended bias on subsequent computational processes thought to support encoding and retrieval—namely pattern separation and completion. Specifically, we found that memory decisions on the current trial influenced memory decisions (experiments 1 and 2) and memory formation (experiment 3) made on the subsequent trial.

Although there is agreement across several hippocampal memory models that encoding

and retrieval should be temporally segregated (13, 23–25), the time required to switch between these processing biases varies widely across models from a few hundred milliseconds (24) to 10 s (12). The current results presented in experiment 2 suggest that the influence of an earlier memory decision decays after a few seconds, consistent with the theoretical time scale of acetylcholine modulation in the hippocampus (12, 14). This result dovetails with the finding that acetylcholine antagonists increase proactive interference (26, 27), a potential consequence of pattern separation failure.

An intriguing open question is whether the lingering nature of the observed memory bias could be an adaptive mechanism to dynamically adjust the criterion for memory reactivation based on the nature of the environment. Rarely do our experiences rapidly switch between the familiar and the novel. Instead, we tend to navigate through situations that generally contain more novel or more familiar components. It could be advantageous for our memory system to be more sensitive to change in new environments and less sensitive to irregularities in familiar environments (25, 28–30). Regardless of the adaptive consequences, the current results shed light on fundamental computational issues of memory encoding and retrieval and highlight that our ongoing processing of the world is influenced by other preceding cognitive operations.

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Supplementary Materials

www.sciencemag.org/cgi/content/full/337/6093/485/DC1
Materials and Methods
Figs. S1 to S8
Tables S1 and S2

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Memory's Penumbra: Episodic Memory Decisions Induce Lingering Mnemonic Biases

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New for Old?

When confronted with a visual stimulus, such as an object or a scene, the brain decides whether it is new, and thus deserves to be encoded as a new memory, or old, which triggers the retrieval of the previously encoded memory. When shown a series of stimuli, some of which are similar to, but not identical to, old memories, it becomes necessary to switch back and forth between encoding and retrieval processing. Using behavioral tasks performed by human test subjects, **Duncan *et al.*** (p. 485) took advantage of the fact that switching takes a second or two and found that a subsequent object, presented before switching has occurred, was more likely to be identified as new when the previous object was new, and identified as old when the previous object was old.

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