

Lingering Cognitive States Shape Fundamental Mnemonic Abilities



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Abstract

Why are people sometimes able to recall associations in exquisite detail while at other times left frustrated by the deficiencies of memory? Although this apparent fickleness of memory has been extensively studied by investigating factors that build strong memory traces, researchers know less about whether memory success also depends on cognitive states that are in place when a cue is encountered. Motivating this possibility, neurocomputational models propose that the hippocampus's capacity to support associative recollection (pattern completion) is biased by persistent neurochemical states, which can be elicited by exposure to familiarity and novelty. We investigated these models' behavioral implications by assessing how recent familiarity influences different memory-retrieval processes. We found that recent familiarity selectively benefitted associative memory (Experiment 1) and that this effect decayed over seconds (Experiment 2), consistent with the timescale of hippocampal neuromodulation. Thus, we show that basic memory computations can be shaped by a subtle, biologically motivated manipulation.

Keywords

memory, novelty, cognition, acetylcholine, open data, open materials

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For memory to be useful, it must go beyond signaling familiar aspects of the world; it must also reactivate previously learned associations. For example, to avoid an embarrassing encounter at a grocery store, you need to both recognize the face of an acquaintance (item memory) and be able to recall his or her name (associative memory). As anyone who has been in this situation can attest, associative memory can be as challenging as it is indispensable. This raises the question: Why do familiar cues evoke detailed memories of a past episode on some occasions but fail to evoke memories on others?

Researchers generally approach this central question by relating memory accuracy to processes evoked by discrete events. This method, however, can reveal only part of the story. It treats each event as though it occurred in isolation, ignoring the ongoing cognitive and neural processes in which they arise. Endel Tulving (1985) first proposed that memory may be influenced by processes unfolding prior to a retrieval cue, postulating that, once reactivated, memories are consciously available only when people are in a neurocognitive attentional state called *retrieval mode*. While there is support for this attentional state (Lepage, Ghaffar,

Nyberg, & Tulving, 2000; Nyberg et al., 1995), the prospect that neurocognitive states can also influence mnemonic reactivation has not been investigated.

To assess this possibility, we turned to computational models that formally characterize how the brain reactivates stored patterns of neural activity. Associative retrieval is mediated in these models through pattern completion, a computational process in which partial cues reactivate stored neural patterns (e.g., Treves & Rolls, 1992). Pattern completion is thought to occur in the hippocampus, a brain structure shown to support associative memory (O'Reilly & McClelland, 1994). Critically, the likelihood of the hippocampus engaging in pattern completion may be biased by shifts in cholinergic input; lower cholinergic input may bias it toward pattern completion, whereas higher cholinergic input may bias it away from pattern completion (Easton, Douchamps, Eacott, & Lever, 2012; Hasselmo & Schnell,

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1994; Hasselmo, Schnell, & Barkai, 1995). This neuro-modulation lasts for seconds, which implies that, once induced, pattern-completion biases also linger for seconds (Hasselmo & Fehrlau, 2001; Meeter, Murre, & Talamini, 2004). The neurocognitive state before encountering retrieval cues could, thus, directly affect the likelihood of pattern completion, irrespective of the strength of the memory traces.

We asked whether this neurocomputational framework can make mechanistic predictions about (a) manipulations that have the power to elicit prolonged neurocognitive states and (b) the specific memory-retrieval processes enhanced by these states. Inspired by a recent study that tested the behavioral consequences of cholinergic models (Duncan, Sadanand, & Davachi, 2012), we assessed whether exposure to familiar versus novel images influences subsequent retrieval of unrelated memories. The crux of this manipulation is that novelty leads to higher acetylcholine release than familiarity does (Giovannini et al., 2001). We reasoned that if behavioral biases also linger for seconds, then recent exposure to familiarity compared with novelty should facilitate pattern-completion-dependent retrieval. We tested this prediction by assessing whether this manipulation influenced associative memory and item memory. As discussed above, retrieving associations (associative memory) is the hallmark of pattern completion. By contrast, there is extensive evidence that simply recognizing a stimulus (item memory) can be supported by extrahippocampal processes (Brown & Aggleton, 2001; Davachi, Mitchell, & Wagner, 2003). Thus, item memory is an excellent foil for associative memory, because it is less dependent on pattern completion.

In Experiment 1, participants made a series of memory judgments about novel and familiar images; each judgment simultaneously assessed associative and item memory. Unbeknownst to the participants, we manipulated whether memory decisions were made shortly after viewing an unrelated familiar or novel image. In Experiment 2, we then measured the time course of familiarity and novelty-evoked mnemonic-processing biases by varying the time between consecutive memory decisions. Together, these experiments revealed that recent mnemonic processing can profoundly shape how people retrieve memories.

Experiment 1

Experiment 1 tested how recent familiarity influences associative- and item-memory retrieval by manipulating whether retrieval judgments were made following novel or unrelated familiar images.

Method

Participants. Thirty-five adults were recruited. Data from 3 participants were excluded from the analyses because they had previously participated in conflicting studies ($n = 2$) or reported drowsiness throughout the experiment ($n = 1$). Including their data did not change the pattern of results. The final analyses included 32 participants (mean age = 18.53 years, range = 18–22). A sample size of 32 was selected prior to data collection using pilot data ($N = 36$). These data were randomly sampled with replacement in a bootstrapping procedure to determine the number of participants required to achieve 80% power. Participants were fluent in English and had no history of psychiatric disorders. They were given course credit for their participation. All experimental procedures were approved by the local ethics committee, and all participants gave written informed consent.

Stimuli. Stimuli consisted of colored images of 242 natural indoor and outdoor scenes and 242 common objects (484 images total), along with three words (“ancient,” “plain,” “safe”). Stimuli were displayed on a gray background on a 21-in. iMac using PsychoPy software (Peirce, 2007).

Procedure. The experiment consisted of an encoding session in which participants associated each image with one of the three words and a retrieval test that simultaneously assessed associative memory for the words and item memory for the images.

Encoding session. During each trial in the encoding session, an image-word pair was displayed on the screen for 3 s (Fig. 1). Images were trial unique, and each image was pseudorandomly paired with one of the three words, such that all three words appeared an equal number of times across the experiment. Participants were asked to vividly imagine a scenario in which the word could describe the image to encourage deep processing of image-word pairs. After the pair disappeared, participants had 1.5 s to rate the imagined scenario on a 4-point continuous scale on the keyboard, using “h” (*very vivid*), “j,” “k,” and “l” (*not vivid at all*). A fixation cross was presented at the center of the screen for 1 s before each trial. A poststudy debriefing session revealed that all participants’ memory-encoding strategies were consistent with the instructions. Participants were informed before the encoding session that their memory would be assessed.

The encoding session was split into eight 3-min blocks. Half the blocks consisted of scene-word pairs, and the remaining blocks consisted of object-word pairs. Scene and object blocks were presented in a counterbalanced alternating order.

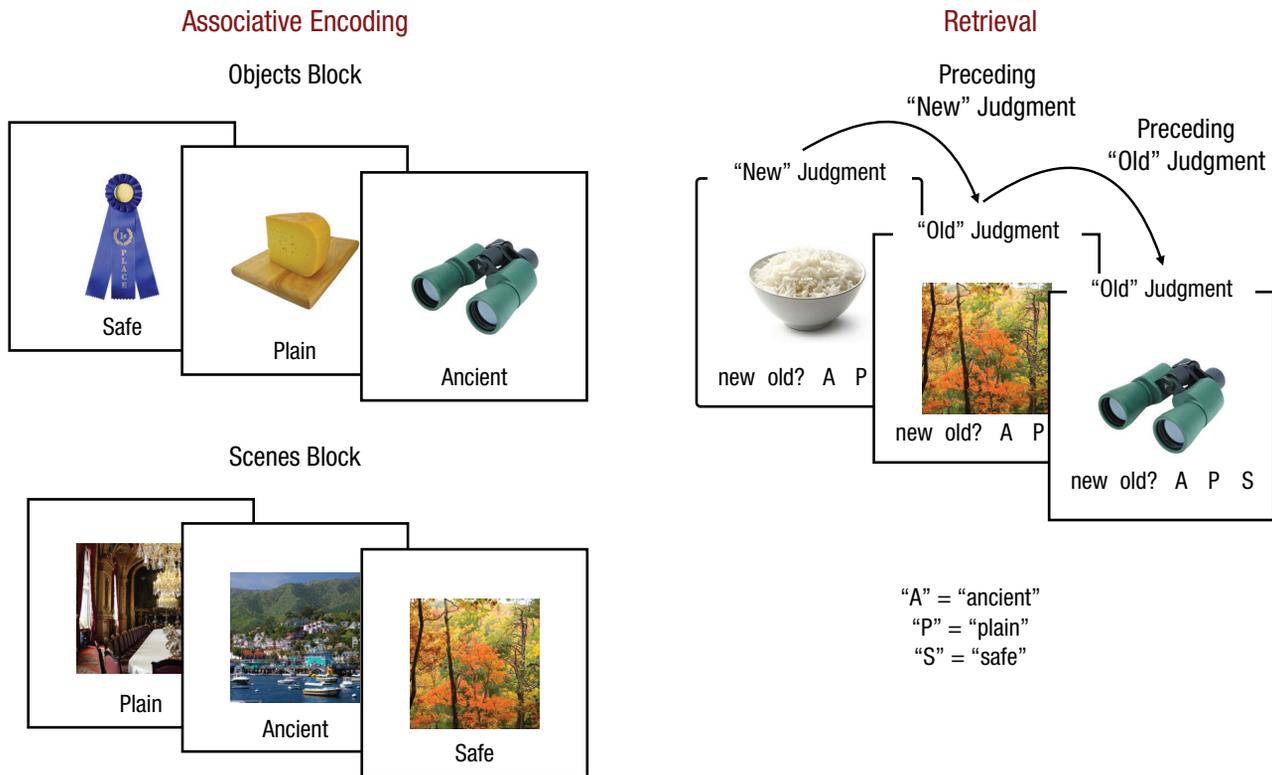


Fig. 1. Sample image-word pairs from the encoding session and illustration of the task in the retrieval session in Experiments 1 and 2. During the associative-encoding session (a), participants saw trial-unique images of objects and scenes during separate blocks. Each image was paired with one of three words (“ancient,” “plain,” “safe”). During retrieval (b), participants saw alternating images of scenes and objects. Images could be old (studied during the encoding session) or new. Participants’ memory for items (images) and associations (words) was tested simultaneously on each trial: They were asked to identify whether the image was new or old, and if old, to indicate whether the word associated with it was “ancient” (“A”), “plain” (“P”), or “safe” (“S”) or whether they could not recollect the associated word (“old?”).

Retrieval session. During the memory test, we assessed participants’ item and associative memory simultaneously. Critically, we manipulated whether participants made each memory decision after an unrelated familiar or novel image. During each retrieval trial, an image was shown on the screen for 2 s. Participants were asked to indicate whether the image was new (by pressing the “d” key) or old, in which case they were asked to recall the word associated with it in the encoding session (by pressing the “j,” “k,” or “l” keys, which corresponded with “ancient,” “plain,” and “safe,” respectively). They were asked to press the “f” key if they thought that an image was old but were unable to recall the associated word (*associative skip*). Note that these response options allowed us to assess participants’ item and associative memory with a single response. The response window was intentionally short, consistent with past research (Duncan et al., 2012), so that (a) memory judgments were made before the mnemonic-processing bias from the preceding trial dissipated and (b) the bias from the preceding trial would not be overcome with sufficient processing time. A central fixation cross was presented during a 1-s interstimulus interval (ISI).

The retrieval session was split into four 6-min blocks. Half of the images presented during the memory test had been previously studied during the encoding session, while the remaining were novel. Critically, scene and object images alternated during the memory test. This reduced the possibility of consecutive old images semantically priming each other, because consecutive images always belonged to different stimulus categories and were, thus, studied during different encoding blocks. Stimulus presentation was predetermined such that no more than four new stimuli appeared consecutively and the transition probability between seeing old and new images was .50.

Data analysis. Corrected associative-memory accuracy and d' ($z(\text{hit rate}) - z(\text{false alarm rate})$), were used to measure associative and item memory, respectively. To obtain independent estimates of associative and item memory, we calculated corrected associative-memory accuracy only for the trials on which participants correctly recognized an image as old (pressing keys other than the “new” response key, i.e., “d”), whereas d' was

calculated only for trials on which participants failed to retrieve the correct association. We corrected for false alarms in associative memory by calculating corrected associative-memory accuracy to account for the three associative response options: corrected associative-memory accuracy = proportion of associative hits – (proportion of associative false alarms/2).

Thus, if a participant randomly made an associative response on each trial, his or her corrected associative-memory accuracy would be $.33 - (.66/2) = 0$. To directly compare associative and item memory as a function of the preceding trial decision, we calculated normalized difference scores—(“old” judgment on preceding trial – “new” judgment on preceding trial)/average memory. Only participants with positive corrected associative-memory accuracy and d' were included in this analysis to avoid negative denominators (1 participant was excluded).

Analyses were conducted using R programming language. Separate 2 (preceding judgment: old vs. new) \times 2 (stimulus: object vs. scene) repeated measures analyses of variance (ANOVAs) were used to analyze corrected associative-memory accuracy, response time on trials on which associative memory was correct, and d' . Paired-samples t tests (two-tailed) were used to examine simple effects. For pairwise comparisons, t tests were conducted with Bonferroni correction. Two generalized mixed-effects models were estimated with an unstructured covariance matrix (glmer function in the lme4 package; Bates, Mächler, Bolker, & Walker, 2014) to control for response time on the preceding trial and preceding trial type, respectively. All models included within-subjects predictors as fixed effects and uncorrelated random intercepts and slopes varying over participant (see the Supplemental Material available online for glmer specification details). Note that the random effects were unstructured in time (no autoregressive structure) and that the “preceding judgment” refers to the judgment given on the preceding trial in the experiment and not the analyzed data frame, which was restricted to recognized “old” trials.

Before any statistical tests were performed, trials for which the correct associative response was the same as the participants’ response on the preceding trial were removed. This was done to reduce response priming. Skipping this correction did not change the pattern of results (see the Supplemental Material).

Results

We first assessed how recent subjective experiences of familiarity and novelty (i.e., the participants’ judgment on the preceding trial) impacted associative memory. Consistent with our hypothesis, results showed that

recent familiarity judgments increased subsequent associative-memory accuracy by a robust 8.23% (95% confidence interval, or CI = [4.10, 12.36]) compared with recent novelty judgments, $F(1, 31) = 13.88$, $p = .001$, $\eta_p^2 = .31$ (Fig. 2a). Although associative-memory accuracy was higher for objects than for scenes, $F(1, 31) = 18.16$, $p < .001$, $\eta_p^2 = .37$, the interaction between preceding judgment and stimulus category was not significant, $F(1, 31) = 1.98$, $p = .169$, $\eta_p^2 = .06$, which underscores the generality of the phenomenon. Preceding familiarity compared with novelty judgments also led to faster retrieval of associations, $F(1, 31) = 7.13$, $p = .012$, $\eta_p^2 = .19$ (see Fig. S3 in the Supplemental Material).

But which aspects of the preceding familiarity drive this associative-memory bias? We first assessed whether the subjective experience of familiarity versus novelty was a better predictor of subsequent associative memory than the objective stimulus familiarity versus novelty (trial type) of the preceding image. Consistent with the importance of the mnemonic experience, results showed that participants’ preceding judgment (subjective) still affected associative-memory accuracy even after adjusting for preceding trial type ($\beta = 0.19$, $z = 2.08$, $p = .038$), but preceding trial type (objective) did not ($\beta = 0.11$, $z = 1.35$, $p = .176$). We next binned trials according to whether participants correctly identified a studied image and retrieved the word associated it (associative) on the preceding trial or correctly recognized the image but failed to retrieve the associated word (item only).

In both conditions, associative memory was improved compared with preceding “new” judgments—item only $>$ new: $t(31) = 4.77$, $p < .001$ (Bonferroni adjusted), 95% CI for the difference between means = [0.07, 0.16], Cohen’s $d = 0.84$; associative $>$ new: $t(31) = 3.17$, $p = .010$ (Bonferroni adjusted), 95% CI for the difference between means = [0.03, 0.14], Cohen’s $d = 0.56$ (see Fig. S1 in the Supplemental Material). However, they did not differ from each other—associative $>$ item only: $t(31) = -0.78$, $p > .250$ (Bonferroni adjusted), 95% CI for the difference between means = [–0.10, 0.04], Cohen’s $d = 0.14$ —which suggests that successful associative retrieval is not required to facilitate associative-memory accuracy on subsequent trials. Lastly, we included response time on the preceding trial as a proxy for difficulty level and found that preceding familiarity judgments influenced associative memory even after controlling for preceding trial difficulty ($\beta = 0.18$, $z = 2.24$, $p = .025$).

Hence, our results demonstrate that recognizing something familiar results in a state that facilitates associative memory, which relies on pattern completion. This, however, leads one to ask: Do all memory-retrieval processes benefit from recent familiarity, or is this benefit

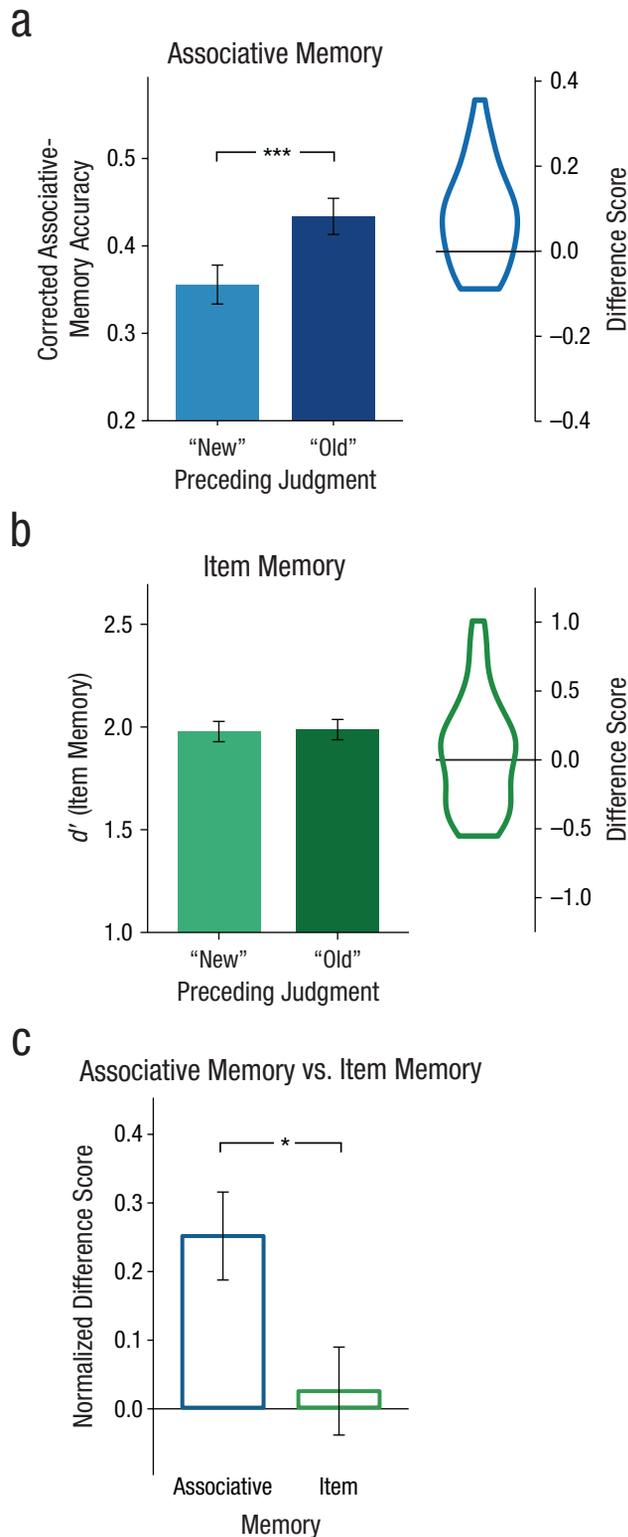


Fig. 2. Results from Experiment 1 ($N = 32$). The bar graphs in (a) and (b) show mean accuracy for associative memory and item memory, respectively, on trials that were preceded by a “new” judgment or an “old” judgment. The violin plots show the distribution of the mean difference score (“old” judgment on preceding trial – “new” judgment on preceding trial) across participants. The bar graph in (c) shows the mean normalized difference score (“old” judgment on preceding trial – “new” judgment on preceding trial/average memory) for associative and item memory. Error bars represent the standard error of the difference between conditions (Morey, 2008). Asterisks indicate significant differences ($*p < .05$, $***p < .001$).

selectively observed for pattern-completion-dependent memory? To investigate this, we analyzed how judgment on a preceding trial influences item memory (d'), which is less dependent on pattern completion. In contrast to the robust associative-retrieval benefit, there was no reliable influence of recent familiarity judgments on item-memory accuracy, $F(1, 31) = 0.02$, $p > .250$, $\eta_p^2 < .01$ (Fig. 2b). There was, however, a main effect of stimulus category, with objects being recognized more than scenes, $F(1, 31) = 52.70$, $p < .001$, $\eta_p^2 = .63$, and an interaction between stimulus category and preceding judgment, $F(1, 31) = 6.38$, $p = .017$, $\eta_p^2 = .17$, with preceding judgments yielding inconsistent, nonsignificant effects across the stimulus categories (see the Supplemental Material for details on stimulus-specific effects). Moreover, the normalized effects of preceding familiarity on associative memory (see the Method for details) were greater than those on item memory—associative > item only, $t(30) = 2.49$, $p = .018$, 95% CI for the difference between means = [0.04, 0.41], Cohen’s $d = 0.45$ (Fig. 2c). Together, these results suggest that recent familiarity does not consistently benefit memory retrieval as a whole; the benefit is selectively seen for pattern-completion-dependent associative memory.

Experiment 2

The results of Experiment 1 suggest that recent familiarity evokes a mnemonic-processing bias that facilitates associative memory. However, they leave two questions unanswered. Firstly, our hypothesis was grounded in cholinergic modulation dynamics, which imply that mnemonic biases would decay within seconds (Hasselmo & Fehrlau, 2001; Meeter et al., 2004). However, we could not measure this decay in Experiment 1 because each trial was separated by a 1-s ISI. Secondly, we could not adjudicate whether recent familiarity facilitated retrieval or recent novelty inhibited it since there was no baseline condition. To answer these questions, we varied the ISI between retrieval trials to (a) measure whether the time course of the mnemonic bias is consistent with cholinergic mechanisms and, if it is, (b) use the longer ISI condition as a baseline to evaluate the relative influence of familiarity and novelty.

Method

Participants. Fifty-one adults were recruited. Data from 3 participants were excluded from the analysis because of low response rates (missed responses $> 4 SD$ above the group mean; $n = 2$) or a high false alarm rate ($> 5 SD$ above the group mean; $n = 1$). Excluding their data did not change the pattern of results. Thus, our final analyses included 48 participants (mean age = 18.40 years, range = 18–22). A sample size of 48 was selected prior to data collection by a power analysis that used a

bootstrapping procedure with Experiment 1 data. We assumed that there would be no influence of preceding familiarity at long ISIs and estimated the number of participants needed to show an interaction between ISI and preceding judgment with 80% power. As in Experiment 1, participants were fluent in English and had no history of psychiatric disorders. They were given course credit for their participation. All experimental procedures were approved by the local ethics committee, and all participants gave written informed consent.

Stimuli and procedure. Stimuli consisted of 196 colored images of natural indoor and outdoor scenes and 196 images of common objects (392 images total), along with three words (“ancient,” “plain,” “safe”). The experimental procedure was similar to that of Experiment 1 except for the following changes. The encoding session was split into six 3-min blocks; three blocks of scene-word pairs and three blocks of object-word pairs were presented in a counterbalanced alternating order. The retrieval session was split into six blocks lasting about 5 min each. Two of those blocks used a 1-s ISI between trials (short), while the remaining four used a 4-s ISI (long). This resulted in an equal number of trials in each ISI condition.

Data analysis. Separate 2 (preceding judgment: old vs. new) \times 2 (stimulus: object vs. scene) \times 2 (ISI: short vs. long) repeated measures ANOVAs were used to analyze corrected associative-memory accuracy, response time for trials on which associative memory was correct, and d' . For the three-way ANOVAs on d' , participants with missing cells were excluded from the analysis ($n = 3$). All but two ANOVAs passed the Shapiro-Wilk normality test (Bonferroni corrected) for each cell in the design. For those that did not pass the test, alternative tests were performed and are reported in the Supplemental Material. In all cases, the inferences held. Paired-samples t tests (two-tailed) were used to examine simple effects. For pairwise comparisons, t tests were conducted with Bonferroni correction. As in Experiment 1, generalized mixed-effects models were estimated with an unstructured covariance matrix (glmer function in the lme4 package; Bates et al., 2014).

Results

Replicating the results of Experiment 1, the analyses showed that associative memory was more accurate following familiar compared with novel judgments across both ISI conditions, $F(1, 47) = 42.98, p < .001, \eta_p^2 = .48$ (Fig. 3a) and that this effect was driven by the recent subjective experience rather than objective familiarity (see the Supplemental Material for control analyses). We also found a main effect of stimulus category,

$F(1, 47) = 47.23, p < .001, \eta_p^2 = .50$. No interactions with stimulus category were significant at the .05 threshold, but we confirmed that preceding judgment influenced associative memory for both objects and scenes to account for a trending three-way interaction, $F(1, 47) = 3.77, p = .058, \eta_p^2 = .07$ (see the Supplemental Material for stimulus-specific effects and additional tests).

In line with the timescale of cholinergic modulation (Hasselmo & Fehrlau, 2001; Meeter et al., 2004), we found a significant two-way interaction between preceding judgment and ISI, $F(1, 47) = 6.53, p = .014, \eta_p^2 = .12$ (Fig. 3a), which indicates that the influence of the preceding judgment decayed over the 4-s ISI. We further unpacked the direction of this interaction and observed that memory performance decreased with time following a trial with familiar stimuli—short ISI $>$ long ISI, $t(47) = 2.41, p = .020$, 95% CI for the difference between means = [0.01, 0.11], Cohen's $d = 0.35$, rather than increasing over time following a trial with novel stimuli—long ISI $>$ short ISI, $t(47) = 1.09, p > .250$, 95% CI for the difference between means = [−0.02, 0.07], Cohen's $d = 0.16$. This suggests that recent familiarity enhances subsequent retrieval rather than that recent novelty inhibits it (Fig. 3a).

Furthermore, the manner in which recent familiarity benefitted pattern-completion-dependent memory was highly selective. Item memory was not influenced by the preceding judgment, $F(1, 44) = 0.61, p > .250, \eta_p^2 = .01$ (see the Supplemental Material for additional tests) or the interaction between ISI and preceding judgment, $F(1, 44) = 0.62, p > .250, \eta_p^2 = .01$ (Fig. 3b). Although item memory was better for objects as opposed to scenes, $F(1, 44) = 61.51, p < .001, \eta_p^2 = .58$, no interactions with stimulus category were significant at the .05 threshold (see the Supplemental Material for stimulus-specific effects). The normalized effects of preceding familiarity on associative memory were significantly greater than those on item memory, $F(1, 46) = 40.24, p < .001, \eta_p^2 = .47$ (Fig. 3c); however, this difference did not decay over time, $F(1, 46) = 2.38, p = .130, \eta_p^2 = .05$. These findings support our hypothesis that recent familiarity selectively facilitates associative-memory retrieval and provide a window into the lingering nature of the mnemonic-processing bias.

Lastly, the high overlap in paradigms between experiments allowed us to combine data and perform several additional control analyses, which would have been underpowered in each experiment alone. In these analyses, we ruled out the following alternative explanations: (a) Near-to-ceiling item-memory performance (see Fig. S6 in the Supplemental Material) obscured item-memory effects, (b) inclusion of the associative-skip option produced spurious results, (c) associative-memory effects

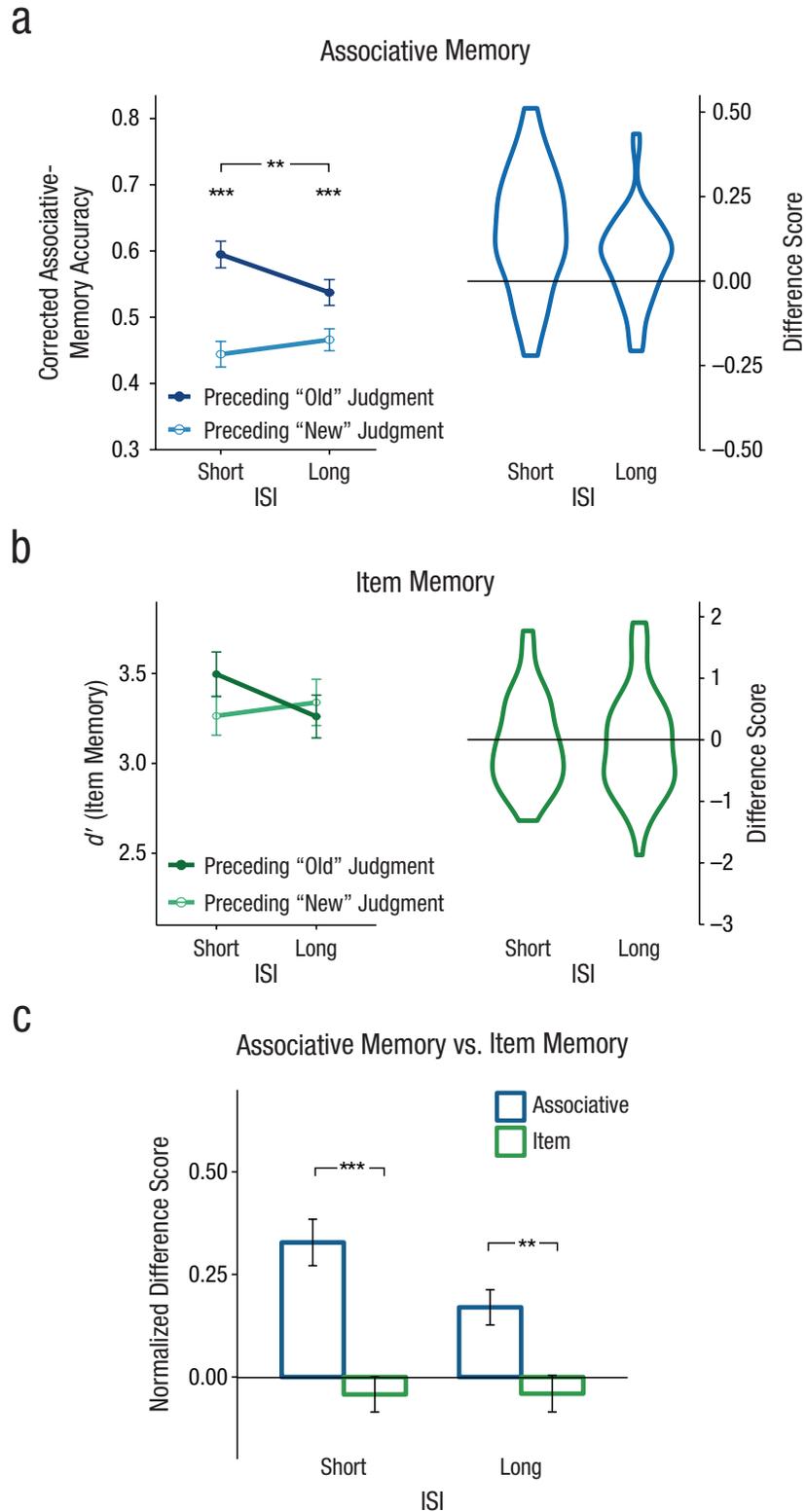


Fig. 3. Results from Experiment 2 ($N = 48$). The line graphs in (a) and (b) show mean accuracy for associative memory and item memory, respectively, as a function of interstimulus interval (ISI) and judgment type on the preceding trial (“old” vs. “new”). The violin plots show the distribution of the mean difference score (“old” judgment on preceding trial – “new” judgment on preceding trial) for each ISI across participants. The bar graph in (c) shows the mean normalized difference score ((“old” judgment on preceding trial – “new” judgment on preceding trial)/average memory) at each ISI, separately for associative and item memory. Error bars represent the standard error of the difference between conditions (Morey, 2008). Asterisks indicate significant differences (** $p < .01$, *** $p < .001$).

were dependent on conditioning the analysis on correct item memory, and (d) the carryover of familiarity caused more retrieval attempts or a tendency to think the next trial involves old items, thereby increasing the rate of associative-retrieval success (see the Supplemental Material for the details of each analysis).

General Discussion

We identified a subtle, biologically motivated manipulation that shapes memory retrieval; after identifying an image as familiar, participants were more likely to retrieve other unrelated associations. This manipulation proved to be extremely powerful, with effect sizes of 0.72 to 0.94—roughly twice the size of the meta-analytical estimates of classic memory-enhancement techniques, such as the testing and generation effects (see meta-analyses in Bertsch, Pesta, Wiscott, & McDaniel, 2007; Rowland, 2014). This difference is particularly striking given that these techniques directly influence the memory itself, whereas our manipulation evoked a processing state that could enhance retrieval of any association. Thus, the effect observed here has the potential to generate particularly flexible applications. Moreover, given that most memory tests include old and new items, these robust effects may permeate existing data sets in which associative memory or recollection was assessed. Uncovering serial dependencies, thus, has important theoretical and pragmatic implications for memory researchers, and we hope that our findings encourage other researchers to investigate these effects in their own work.

We interpret the benefits of recent familiarity as evidence for a memory state rather than evidence for primed content, because we minimized the contextual overlap between consecutive retrieval trials. Specifically, the preceding trial was always from a different stimulus category and was encoded during a different block. Similarly, to reduce response priming, we removed trials on which the correct associative response was the same as the preceding judgment. The only remaining contextual overlap was the encoding context, which was shared across all memories. However, the sheer number of encoded images make it unlikely that overlapping context would effectively cue the memory tested on the subsequent trial, especially given that so many other memories had more related content and temporal context. Lastly, follow-up analyses also revealed that the preceding trial's difficulty could not explain the influence of recent familiarity. Thus, the most parsimonious explanation of the results is that recent familiarity, *per se*, influenced subsequent memory performance.

These results can be accounted for by neurocomputational models (Hasselmo & Schnell, 1994; Hasselmo et al., 1995; Hasselmo, Wyble, & Wallenstein, 1996). Hippocampal pattern completion is thought to support associative retrieval by reactivating neural patterns of activity elicited by prior related experiences, essentially increasing the similarity between current and earlier event representations (O'Reilly & McClelland, 1994). While this process may be crucial for associative retrieval, it could also be deleterious for other mnemonic operations, such as forming distinct memory traces. Interference could be reduced through the complementary hippocampal process of pattern separation, which decreases the overlap between representations. Thus, the fundamental mnemonic processes of pattern completion and separation are computationally incompatible (O'Reilly & McClelland, 1994). Cholinergically mediated mnemonic states could allow the hippocampus to deal with competing demands by prioritizing one process over the other at adaptive times (Hasselmo et al., 1995; Hasselmo et al., 1996). Relatively higher cholinergic innervation of the hippocampus in the presence of novelty as opposed to familiarity could bias the networks toward pattern separation, preparing the hippocampus to form distinct representations. Conversely, in the presence of familiarity as opposed to novelty, lower cholinergic input could bias the networks toward pattern completion, preparing the hippocampus to retrieve associations. Empirical research supports the mnemonic consequences of cholinergic shifts (Atri et al., 2004; De Rosa & Hasselmo, 2000; Douchamps, Jeewajee, Blundell, Burgess, & Lever, 2013) and the relative decrease in cholinergic innervation in familiar compared with novel contexts (Giovannini et al., 2001), but it is less clear whether novelty or familiarity triggers this shift. The results of Experiment 2 are most consistent with a familiarity-driven mechanism, and further characterization of cholinergic signaling in the hippocampus could determine whether it is also familiarity driven.

Cholinergic models of hippocampal function predict that pattern-separation-dependent memory should be enhanced by novelty. Working within this framework, Duncan and colleagues (2012) showed that novelty evoked a pattern-separation bias that lasted for seconds, influencing subsequent retrieval decisions. Our study provides an important extension to Duncan et al.'s results by investigating whether pattern-completion biases can be established by familiarity. The double dissociation between our results and Duncan et al.'s provides strong evidence that familiarity and novelty have selective effects on memory retrieval, affecting performance on the basis of the computational demands of the task at hand.

Although our results closely parallel hippocampal cholinergic mechanisms, alternative mechanisms should be considered. For example, novelty also elicits the release of dopamine and norepinephrine throughout the brain, and these neurochemicals, in conjunction with acetylcholine, could impact memory performance. There are two key reasons, however, for favoring our cholinergic interpretation. First, the time course of the effects is most consistent with cholinergic mechanisms (Hasselmo & Fehrlau, 2001; Meeter et al., 2004): Dopamine's influence on memory lasts for minutes rather than decaying over seconds (Bethus, Tse, & Morris, 2010; O'Carroll, Martin, Sandin, Frenguelli, & Morris, 2006). Second, all other accounts would predict better performance following novelty, when the concentration of each neurochemical is highest. For example, norepinephrine has been associated with enhanced memory retrieval (Murchison et al., 2004). Moreover, cortical cholinergic modulation has been associated with increased attention (e.g., Furey, Pietrini, Haxby, & Drevets, 2008) and item recognition (Winters & Bussey, 2005) but not associative memory (Barker & Warburton, 2009). While hard to reconcile with the associative-memory findings, the novelty-related enhancements predicted by these other forms of neuromodulation may contribute to item-memory performance; perhaps the inconsistent and small influence of preceding decisions on item memory reflects the net enhancements of recent familiarity on recollection (without the associated word) and recent novelty on attention and cortical item-recognition signals. This may explain the trend toward stimulus-specific item-memory effects in Experiment 1, because memory of different stimulus classes could differentially depend on these processes, but this possibility is undermined by Experiment 2 showing qualitatively different stimulus-specific patterns.

Whereas our hypothesis was driven by neurocomputational models, Tulving (1985) first proposed the existence of a "retrieval mode," which he conceptualized as an attentional state that allowed mental time travel to a particular "episode." The retrieval mode specifically permits conscious access to memories recovered through *ecphory* or pattern completion. If it takes time to enter into a retrieval mode, this process could also result in sequential dependencies, for example, when switching between semantic and episodic retrieval (Herron & Wilding, 2006). The effect of recent familiarity reported here, however, is better accounted for by a mnemonic-processing bias that directly influences *ecphory* or pattern completion rather than retrieval mode: Whereas Tulving's retrieval mode is strategic and goal-directed, our poststudy debriefing indicated that familiarity evoked mnemonic states without conscious

awareness. Tulving's retrieval mode would also apply equally to recognizing familiar items and recalling associated details; in fact, many studies that assessed the theory used old/new recognition judgments (Lepage et al., 2000; Nyberg et al., 1995). Moreover, a retrieval mode is required to both recognize old cues and detect novel ones; thus, participants likely engaged in retrieval mode to a similar degree in each preceding condition. One could argue that retrieval mode is abandoned following novelty detection, which reduces retrieval performance on the subsequent trial. However, retrieval mode is just as likely to also be abandoned following successful retrieval. Further, this argument still cannot account for a dissociation between associative and item memory. Thus, while additional neuroimaging research is required, our results are best explained by recent familiarity facilitating the reactivation of stored memories than evoking a controlled attentional mode.

In conclusion, our results demonstrate that processes unfolding prior to stimulus presentation can have profound behavioral consequences. A growing body of research demonstrates that prestimulus neural activity influences memory (Addante, Watrous, Yonelinas, Ekstrom, & Ranganath, 2011; Otten, Quayle, & Puvaneswaran, 2010; Park & Rugg, 2010), which underscores the importance of neural states for cognition. Whereas much of this emerging field has focused on spontaneous activity, our work identifies factors that may elicit prestimulus states, thereby opening the door for interventions that can harness mnemonic states to create tailored learning environments.

Action Editor

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Author Contributions

Both authors contributed to the study concept and design, drafted the manuscript, and approved the final version for submission. A. Patil analyzed and collected the data under the supervision of K. Duncan.

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Declaration of Conflicting Interests

The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

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Supplemental Material

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Open Practices



All data and materials have been made publicly available via the Open Science Framework and can be accessed at <https://osf.io/d7w8a/>. The complete Open Practices Disclosure for this article can be found at <http://journals.sagepub.com/doi/suppl/10.1177/0956797617728592>. This article has received badges for Open Data and Open Materials. More information about the Open Practices badges can be found at <http://www.psychologicalscience.org/publications/badges>.

References

- Addante, R., Watrous, A., Yonelinas, A., Ekstrom, A., & Ranganath, C. (2011). Prestimulus theta activity predicts correct source memory retrieval. *Proceedings of the National Academy of Sciences, USA*, *108*, 10702–10707.
- Atri, A., Sherman, S., Norman, K. A., Kirchoff, B. A., Nicolas, M. M., Greicius, M. D., . . . Stern, C. E. (2004). Blockade of central cholinergic receptors impairs new learning and increases proactive interference in a word paired-associate memory task. *Behavioral Neuroscience*, *118*, 223–236. doi:10.1037/0735-7044.118.1.223
- Barker, G. R. I., & Warburton, E. C. (2009). Critical role of the cholinergic system for object-in-place associative recognition memory. *Learning & Memory*, *16*, 8–11.
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *arXiv preprint arXiv:1406.5823*.
- Bertsch, S., Pesta, B. J., Wiscott, R., & McDaniel, M. A. (2007). The generation effect: A meta-analytic review. *Memory & Cognition*, *35*, 201–210.
- Bethus, I., Tse, D., & Morris, R. (2010). Dopamine and memory: Modulation of the persistence of memory for novel hippocampal NMDA receptor-dependent paired associates. *The Journal of Neuroscience*, *30*, 1610–1618.
- Brown, M. W., & Aggleton, J. P. (2001). Recognition memory: What are the roles of the perirhinal cortex and hippocampus? *Nature Reviews Neuroscience*, *2*, 51–61.
- Davachi, L., Mitchell, J. P., & Wagner, A. D. (2003). Multiple routes to memory: Distinct medial temporal lobe processes build item and source memories. *Proceedings of the National Academy of Sciences, USA*, *100*, 2157–2162.
- De Rosa, E., & Hasselmo, M. E. (2000). Muscarinic cholinergic neuromodulation reduces proactive interference between stored odor memories during associative learning in rats. *Behavioral Neuroscience*, *114*, 32–41. doi:10.1037/0735-7044.114.1.32
- Douchamps, V., Jeewajee, A., Blundell, P., Burgess, N., & Lever, C. (2013). Evidence for encoding versus retrieval scheduling in the hippocampus by theta phase and acetylcholine. *The Journal of Neuroscience*, *33*, 8689–8704. doi:10.1523/JNEUROSCI.4483-12.2013
- Duncan, K., Sadanand, A., & Davachi, L. (2012). Memory's penumbra: Episodic memory decisions induce lingering mnemonic biases. *Science*, *337*, 485–487.
- Easton, A., Douchamps, V., Eacott, M., & Lever, C. (2012). A specific role for septohippocampal acetylcholine in memory? *Neuropsychologia*, *50*, 3156–3168.
- Furey, M., Pietrini, P., Haxby, J., & Drevets, W. (2008). Selective effects of cholinergic modulation on task performance during selective attention. *Neuropsychopharmacology*, *33*, 913–923.
- Giovannini, M., Rakovska, A., Benton, R., Pazzagli, M., Bianchi, L., & Pepeu, G. (2001). Effects of novelty and habituation on acetylcholine, GABA, and glutamate release from the frontal cortex and hippocampus of freely moving rats. *Neuroscience*, *106*, 43–53.
- Hasselmo, M. E., & Fehrlau, B. (2001). Differences in time course of ACh and GABA modulation of excitatory synaptic potentials in slices of rat hippocampus. *Journal of Neurophysiology*, *86*, 1792–1802.
- Hasselmo, M. E., & Schnell, E. (1994). Laminar selectivity of the cholinergic suppression of synaptic transmission in rat hippocampal region CA1: Computational modeling and brain slice physiology. *The Journal of Neuroscience*, *14*, 3898–3914.
- Hasselmo, M. E., Schnell, E., & Barkai, E. (1995). Dynamics of learning and recall at excitatory recurrent synapses and cholinergic modulation in rat hippocampal region CA3. *The Journal of Neuroscience*, *15*, 5249–5262.
- Hasselmo, M. E., Wyble, B. P., & Wallenstein, G. V. (1996). Encoding and retrieval of episodic memories: Role of cholinergic and GABAergic modulation in the hippocampus. *Hippocampus*, *6*, 693–708.
- Herron, J. E., & Wilding, E. L. (2006). Brain and behavioral indices of retrieval mode. *NeuroImage*, *32*, 863–870.
- Lepage, M., Ghaffar, O., Nyberg, L., & Tulving, E. (2000). Prefrontal cortex and episodic memory retrieval mode. *Proceedings of the National Academy of Sciences, USA*, *97*, 506–511.
- Meeter, M., Murre, J. M. J., & Talamini, L. M. (2004). Mode shifting between storage and recall based on novelty detection in oscillating hippocampal circuits. *Hippocampus*, *14*, 722–741.
- Morey, R. D. (2008). Confidence intervals from normalized data: A correction to Cousineau (2005). *Tutorials in Quantitative Methods for Psychology*, *4*, 61–64.
- Murchison, C. F., Zhang, X.-Y., Zhang, W.-P., Ouyang, M., Lee, A., & Thomas, S. A. (2004). A distinct role for norepinephrine in memory retrieval. *Cell*, *117*, 131–142.
- Nyberg, L., Tulving, E., Habib, R., Nilsson, L. G., Kapur, S., Houle, S., . . . McIntosh, A. (1995). Functional brain maps of retrieval mode and recovery of episodic information. *NeuroReport*, *7*, 249–252.
- O'Carroll, C. M., Martin, S. J., Sandin, J., Frenguelli, B., & Morris, R. G. M. (2006). Dopaminergic modulation of the

- persistence of one-trial hippocampus-dependent memory. *Learning & Memory*, *13*, 760–769.
- O'Reilly, R., & McClelland, J. L. (1994). Hippocampal conjunctive encoding, storage, and recall: Avoiding a trade-off. *Hippocampus*, *4*, 661–682.
- Otten, L. J., Quayle, A. H., & Puvaneswaran, B. (2010). Pre-stimulus subsequent memory effects for auditory and visual events. *Journal of Cognitive Neuroscience*, *22*, 1212–1223.
- Park, H., & Rugg, M. D. (2010). Prestimulus hippocampal activity predicts later recollection. *Hippocampus*, *20*, 24–28.
- Peirce, J. W. (2007). PsychoPy—Psychophysics software in Python. *Journal of Neuroscience Methods*, *162*, 8–13.
- Rowland, C. A. (2014). The effect of testing versus restudy on retention: A meta-analytic review of the testing effect. *Psychological Bulletin*, *140*, 1432–1463.
- Treves, A., & Rolls, E. T. (1992). Computational constraints suggest the need for two distinct input systems to the hippocampal CA3 network. *Hippocampus*, *2*, 189–199.
- Tulving, E. (1985). How many memory systems are there? *American Psychologist*, *40*, 385–398.
- Winters, B. D., & Bussey, T. J. (2005). Removal of cholinergic input to perirhinal cortex disrupts object recognition but not spatial working memory in the rat. *European Journal of Neuroscience*, *21*, 2263–2270.