

Research

Category-specific memory encoding in the medial temporal lobe and beyond: the role of reward

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The medial temporal lobe (MTL), including the hippocampus (HC), perirhinal cortex (PRC), and parahippocampal cortex (PHC), is central to memory formation. Reward enhances memory through interplay between the HC and substantia nigra/ventral tegmental area (SNVTA). While the SNVTA also innervates the MTL cortex and amygdala (AMY), their role in reward-enhanced memory is unclear. Prior research suggests category specificity in the MTL cortex, with the PRC and PHC processing object and scene memory, respectively. It is unknown, however, whether reward modulates category-specific memory processes. Furthermore, no study has demonstrated clear category specificity in the MTL for encoding processes contributing to subsequent recognition memory. To address these questions, we had 39 healthy volunteers (27 for all memory-based analyses) undergo functional magnetic resonance imaging while performing an incidental encoding task pairing objects or scenes with high or low reward, followed by a next-day recognition test. Behaviorally, high reward preferably enhanced object memory. Neural activity in the PRC and PHC reflected successful encoding of objects and scenes, respectively. Importantly, AMY encoding effects were selective for high-reward objects, with a similar pattern in the PRC. The SNVTA and HC showed no clear evidence of successful encoding. This behavioral and neural asymmetry may be conveyed through an anterior–temporal memory system, including the AMY and PRC, potentially in interplay with the ventromedial prefrontal cortex.

[Supplemental material is available for this article.]

The ability to turn experiences into new memories is a central part of life. Beginning with the famous patient H.M. in the 1950s (Scoville and Milner 1957), a large body of research indicates a critical role for the medial temporal lobe (MTL), with its subregions hippocampus (HC), perirhinal cortex (PRC), and parahippocampal cortex (PHC), in memory (Zola-Morgan and Squire 1990; Eichenbaum et al. 2007; Squire and Zola-Morgan 2011). How does the MTL contribute to successful memory formation? The dopaminergic reward system, to which the MTL is densely connected (Haber and Knutson 2010; Shohamy and Adcock 2010; Miendlarzewska et al. 2016), plays a key role. Lisman and Grace (2005) described a mechanism in which the HC and dopaminergic system interact to encode new long-term memories. Here, HC novelty signals are relayed via the ventral striatum (VS) to the dopaminergic midbrain, where they trigger a dopamine response that in turn promotes long-term potentiation in the HC (Lisman and Grace 2005). In humans, reward enhances memory formation, accompanied by functional modulations of the HC and dopaminergic midbrain (substantia nigra/ventral tegmental area [SNVTA]) (Wittmann et al. 2005; Adcock et al. 2006; Bunzeck et al. 2012; Wolosin et al. 2012; Murty and Adcock 2014; Miendlarzewska et al. 2016).

Importantly, not only the HC but also the MTL cortex and adjacent amygdala (AMY) are innervated by the SNVTA (Beckstead et al. 1979; Scatton et al. 1980; Insausti et al. 1987; Oades and Halliday 1987) and connected to other regions of the reward network, including the ventromedial prefrontal cortex (vmPFC) (Russchen and Price 1984; Amaral and Insausti 1992; Carmichael

and Price 1995; McIntyre et al. 1996; Kondo et al. 2005; Kondo and Witter 2014). How do these extrahippocampal regions contribute to reward enhancement of memory formation? A possible answer comes from a largely separate line of MTL memory research emphasizing category specificity. Here, the MTL input/output regions PRC and PHC are thought to preferentially process object-related and spatial information, respectively (Davachi 2006; Eichenbaum et al. 2007), due to their differential connectivity to the ventral and dorsal visual stream (Suzuki and Amaral 1994a; Burwell and Amaral 1998a). These object-related and spatial information streams are then relayed, both directly and via the entorhinal cortex (EC), to the HC, where they converge (Witter and Amaral 1991; Suzuki and Amaral 1994b; Burwell and Amaral 1998b; Lavenex and Amaral 2000). In this account, the HC's role in memory is therefore thought to be associative and category-independent (Davachi 2006; Eichenbaum et al. 2007).

However, these two lines of research—reward enhancement of memory and category specificity—have never been jointly investigated. It is therefore unclear whether reward enhances memory formation for objects and scenes in a category-independent way through hippocampal mechanisms and/or in a category-specific way through modulation of the MTL cortex. The PRC and AMY may play a unique role in reward-enhanced memory formation: The PRC may link object features to reward information

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(Miyashita 2019), and the PRC and AMY are both parts of a hypothesized “anterior temporal system” (AT) that is thought to represent the (motivational) salience of unitized entities such as objects (Ranganath and Ritchey 2012; Ritchey et al. 2015). Indeed, another strong behavioral motivator—emotion—may selectively enhance encoding of items in the PRC and AMY but not encoding of contexts in the PHC and HC (Ritchey et al. 2019). In turn, item versus context dissociations in the MTL may be tied to object-related versus spatial processing (Davachi 2006). It follows that reward modulation of neural memory formation may be at least in part category-specific.

Two seminal fMRI studies on the reward enhancement of memory formation (Wittmann et al. 2005; Adcock et al. 2006) have investigated encoding processes contributing to subsequent recognition memory (which may be distinct from encoding of associations or contexts) (Ritchey et al. 2019). While it is currently unknown whether such subsequent recognition memory effects in the MTL—regardless of reward—are category-specific, there are strong reasons to expect this. Functional imaging studies have localized object-related and spatial processing to the PRC and PHC, respectively, during a range of tasks including perception (Litman et al. 2009; Liang et al. 2013; Berron et al. 2018), associative encoding (Awipi and Davachi 2008; Staresina et al. 2011), associative retrieval (Staresina et al. 2012, 2013; Mack and Preston 2016; Schultz et al. 2019, 2022), short-term memory reactivation (Schultz et al. 2012), and recognition-based retrieval (Martin et al. 2013; Kafkas et al. 2017), although there are reports that these regions may also contribute to processing of their nonpreferred category (e.g., Adcock et al. 2006; Preston et al. 2010; Wolosin et al. 2012, 2013; Schultz et al. 2019). It is unclear, however, whether this putative object-related versus spatial distinction in the PRC versus PHC generalizes to encoding processes contributing to subsequent recognition memory. There are numerous reports of PRC involvement in subsequent recognition memory, albeit not in a category-specific manner (Davachi et al. 2003; Ranganath et al. 2004; Staresina and Davachi 2008; Preston et al. 2010), whereas the PHC has been implicated in scene-specific subsequent recognition memory (Prince et al. 2009; Preston et al. 2010).

Hence, we have identified two open questions. (1) Does reward modulate neural processes of memory encoding in a category-specific way? (2) Does the category-specific dissociation between the PRC and PHC extend to encoding processes contributing to subsequent recognition memory, regardless of reward? To close these gaps in the literature, we investigated the neural effects of successful memory encoding for two categories (objects and scenes), fully crossed with two reward magnitudes (high and low). Thirty-nine participants (27 for all memory-based analyses) underwent functional magnetic resonance imaging (fMRI) while they solved an incidental encoding task. Each trial presented an object or scene with a yellow or blue frame. Participants responded whether this category–frame combination predicted high or low reward (combinations were instructed before each run). Correct responses were always followed with high- or low-reward feedback, respectively. One day later, participants returned to the laboratory for an unscanned surprise recognition memory test. Here, the same objects and scenes were presented intermixed with novel distractor images. For each image, participants first indicated whether it was “new” or “old,” followed by the remember–know procedure, which separates the influences of two putative recognition memory processes: recollection and familiarity (Tulving 1985; Yonelinas et al. 2010). Behaviorally, we expected high reward to improve memory for both objects and scenes. For the fMRI data, we expected activity in the MTL, AMY, and SNVTA to reflect this reward-enhanced encoding. Specifically, we expected these effects to be category-independent in the HC and SNVTA and category-specific in the PRC/AMY for objects and in the PHC for scenes.

Results

Unless noted otherwise, the below analyses are based on a subsample of $n = 27$ (“memory sample”) selected for their memory performance out of $n = 39$ participants (“full sample”) (see the Materials and Methods for selection procedure).

Behavioral results

Incidental encoding task

First, we analyzed whether participants correctly identified high versus low reward in the incidental encoding task for our conditions (objects–high reward [OB-HI], objects–low reward [OB-LO], scenes–high reward [SC-HI], and scenes–low reward [SC-LO]). As planned, accuracy was near ceiling (mean [SEM] percentage accuracy: OB-HI: 98.5 [0.4], OB-LO: 98.4 [0.4], SC-HI: 97.0 [0.7], and SC-LO: 97.8 [0.5]). A repeated measures ANOVA with the factors of image category and reward showed a significant effect of category (objects > scenes, $F_{(1,26)} = 5.111$, $P = 0.032$), but no effect of reward or interaction of category and reward ($P \geq 0.212$). Importantly, only trials with accurate responses in the encoding task were considered in subsequent analyses.

Recognition task

For the recognition task, we expected improved subsequent memory in the high-reward condition compared with the low-reward condition for both objects and scenes (see Table 1; Fig. 1A). We first analyzed corrected hit rate (CHR; hit rate minus false alarm rate) for each condition. A repeated measures ANOVA yielded a main effect of reward (high > low, $F_{(1,26)} = 18.297$, $P < 0.001$) and, unexpectedly, a main effect of category (objects > scenes, $F_{(1,26)} = 7.404$, $P = 0.011$), as well as an interaction effect of category and reward ($F_{(1,26)} = 9.961$, $P = 0.004$), indicating greater reward enhancement of object compared with scene memory. Follow-up paired t -tests showed that high-reward objects were remembered better than low-reward objects (OB-HI > OB-LO, $t_{(26)} = 5.568$, $P < 0.001$), while high-reward scenes were remembered better than low-reward scenes on a trend level only (SC-HI > SC-LO, $t_{(26)} = 1.759$, $P = 0.090$). We also explored whether these results reflected a systematic difference between objects and scenes, which should be apparent in both the high-reward and low-reward conditions. However, the difference between objects and scenes was only significant in the high-reward condition (OB-HI vs. SC-HI, $t_{(26)} = 3.590$, $P = 0.001$) but not in the low-reward condition (OB-LO vs. SC-LO, $t_{(26)} = 0.596$, $P = 0.556$), indicating that the observed main effect of category was driven by the interaction effect.

Additional analyses explored whether the observed memory effects were specific to a memory process (recollection or familiarity) (see the Materials and Methods) or sample (memory subsample as in the analyses above [$n = 27$] or full sample [$n = 39$]). Importantly, all memory measures (CHR, recollection, and familiarity) at both sample sizes showed the observed interaction between category and reward in the same direction, with greater reward enhancement of object memory than scene memory (see Table 1).

Analyses of the source memory task are included in the Supplemental Material (see Supplemental Table S1).

fMRI: ROI results—category, subsequent memory, and the role of reward

First, we analyzed whether reward modulated memory encoding for objects and scenes in our ROIs (model 1, memory subsample). To this end, the factors category (OB [objects] and SC [scenes]), reward (HI [high] and LO [low]), and subsequent memory

Table 1. Overview over recognition memory results

Outcome	OB-HI	OB-LO	SC-HI	SC-LO	Effect of category	Effect of reward	Interaction
CHR ^a	0.382 (0.023)	0.295 (0.017)	0.317 (0.020)	0.287 (0.018)	$F_{(1,26)} = 7.404$, $P = 0.011$	$F_{(1,26)} = 18.297$, $P < 0.001$	$F_{(1,26)} = 9.961$, $P = 0.004$
CHR ^b	0.330 (0.022)	0.222 (0.023)	0.254 (0.023)	0.231 (0.020)	$F_{(1,38)} = 4.386$, $P = 0.043$	$F_{(1,38)} = 29.980$, $P < 0.001$	$F_{(1,38)} = 26.278$, $P < 0.001$
Recollection ^a	0.194 (0.021)	0.124 (0.015)	0.138 (0.021)	0.117 (0.018)	$F_{(1,26)} = 3.209$, $P = 0.085$	$F_{(1,26)} = 18.711$, $P < 0.001$	$F_{(1,26)} = 10.018$, $P = 0.004$
Recollection ^b	0.173 (0.017)	0.103 (0.012)	0.118 (0.016)	0.106 (0.014)	$F_{(1,38)} = 3.903$, $P = 0.055$	$F_{(1,38)} = 19.582$, $P < 0.001$	$F_{(1,38)} = 13.536$, $P < 0.001$
Familiarity ^a	1.016 (0.092)	0.800 (0.075)	0.836 (0.077)	0.777 (0.072)	$F_{(1,26)} = 1.949$, $P = 0.175$	$F_{(1,26)} = 9.482$, $P = 0.005$	$F_{(1,26)} = 6.372$, $P = 0.018$
Familiarity ^b	0.868 (0.078)	0.598 (0.077)	0.663 (0.074)	0.584 (0.071)	$F_{(1,38)} = 3.376$, $P = 0.074$	$F_{(1,38)} = 19.642$, $P < 0.001$	$F_{(1,38)} = 14.603$, $P < 0.001$

The recognition memory results demonstrate consistent effects of our experimental manipulations across all outcome measures at both sample sizes. The table contains mean (SEM) values for all four conditions as well as F -values and P -values from two-way repeated measures ANOVAs with the factors category and reward.

^aMemory sample ($n = 27$).

^bFull sample ($n = 39$).

(H [hit] and M [miss]) were combined into eight conditions of interest: OB-HI-H, OB-HI-M, OB-LO-H, OB-LO-M, SC-HI-H, SC-HI-M, SC-LO-H, and SC-LO-M. Beta values for each condition were averaged across all voxels of each ROI (HC, PRC, PHC, AMY, and SNVTA). These values were then submitted to a four-way repeated measures ANOVA with the factors ROI, category, reward, and subsequent memory. We report interactions of the ROI factor with any experimental factors. This analysis revealed significant two-way interactions of ROI with category ($F_{(1,80,46,86)} = 133.036$, $P < 0.001$) and memory ($F_{(3,30,85,71)} = 9.819$, $P < 0.001$), a three-way interaction of ROI with category and memory ($F_{(3,12,80,99)} = 6.493$, $P < 0.001$), and a four-way interaction of ROI with category, reward, and memory ($F_{(3,55,92,21)} = 3.228$, $P = 0.020$). The interaction of ROI with reward was marginally significant ($F_{(2,55,66,25)} = 2.880$, $P = 0.051$). There were no other interaction effects involving the ROI factor (all $P \geq 0.511$).

Given the significant four-way interaction of ROI, category, reward, and memory, we computed individual three-way ANOVAs within each ROI as well as follow-up tests where appropriate. A summary of results for each ROI is shown in Figure 1B.

HC

The HC showed a significant main effect of category (scenes > objects, $F_{(1,26)} = 70.192$, $P < 0.001$). No other main effect or interaction was significant (all $P \geq 0.207$).

PRC

The PRC showed significant main effects of category (objects > scenes, $F_{(1,26)} = 10.557$, $P = 0.003$) and subsequent memory (hits > misses, $F_{(1,26)} = 5.840$, $P = 0.023$). Importantly, the interaction of category and subsequent memory was also significant ($F_{(1,26)} = 6.558$, $P = 0.017$), indicating that subsequent memory effects were stronger for objects than scenes. No other main or interaction effect was significant (all $P \geq 0.118$). To explore which conditions showed subsequent memory effects, we additionally computed paired t -tests between subsequent hits and misses for OB-HI, OB-LO, SC-HI, and SC-LO. Notably, only the subsequent memory effect for OB-HI was significant ($t_{(26)} = 3.036$, $P = 0.005$, all other $P \geq 0.412$).

PHC

The PHC showed significant main effects of category (scenes > objects, $F_{(1,26)} = 153.697$, $P < 0.001$) and subsequent memory (hits >

misses, $F_{(1,26)} = 29.407$, $P < 0.001$). Importantly, the interaction of category and subsequent memory was also significant ($F_{(1,26)} = 6.372$, $P = 0.018$), indicating that subsequent memory effects were stronger for scenes than objects. Additionally, we observed a significant main effect of reward (high > low, $F_{(1,26)} = 10.391$, $P = 0.003$), as well as a significant interaction effect of category and reward (greater reward effect for scenes than objects, $F_{(1,26)} = 4.658$, $P = 0.040$). Again, we explored which conditions showed subsequent memory effects using pairwise t -tests between subsequent hits and misses. We observed significant effects of subsequent memory for both SC-HI and SC-LO ($t_{(26)} = [3.788, 3.998]$, $P < 0.001$) but not for either OB-HI or OB-LO (all $P \geq 0.181$).

AMY

The AMY showed a significant main effect of subsequent memory (hits > misses, $F_{(1,26)} = 7.040$, $P = 0.013$) as well as a significant three-way interaction of category, reward, and subsequent memory ($F_{(1,26)} = 4.369$, $P = 0.047$). To identify the constituents of this three-way interaction, we computed separate two-way ANOVAs (reward and memory) for objects and scenes, respectively. For objects, the AMY showed a significant main effect of subsequent memory ($F_{(1,26)} = 4.852$, $P = 0.037$) and, importantly, a significant interaction effect of reward and subsequent memory ($F_{(1,26)} = 7.183$, $P = 0.013$). The main effect of reward was not significant ($P = 0.794$). For scenes, the AMY showed a significant main effect of subsequent memory ($F_{(1,26)} = 4.323$, $P = 0.048$) but no main effect of reward or interaction of reward and subsequent memory ($P \geq 0.651$). Again, we explored which conditions showed subsequent memory effects using pairwise t -tests between subsequent hits and misses. Notably, only the subsequent memory effect for OB-HI was significant ($t_{(26)} = 3.385$, $P = 0.002$, all other $P \geq 0.101$).

SNVTA

Contrary to our expectations, the SNVTA showed no significant main effects or interactions, save for a trend-level three-way interaction of category, reward, and subsequent memory ($F_{(1,26)} = 2.957$, $P = 0.097$, all other $P \geq 0.315$).

Please see the **Supplemental Material** for the following additional analyses: (1) as above but using only “remember” trials rather than all hit trials (see **Supplemental Fig. S1**), (2) as above (model 1) but within the anterior HC only (see **Supplemental Fig. S2**), and (3) whole-brain contrasts of the category-specific subsequent

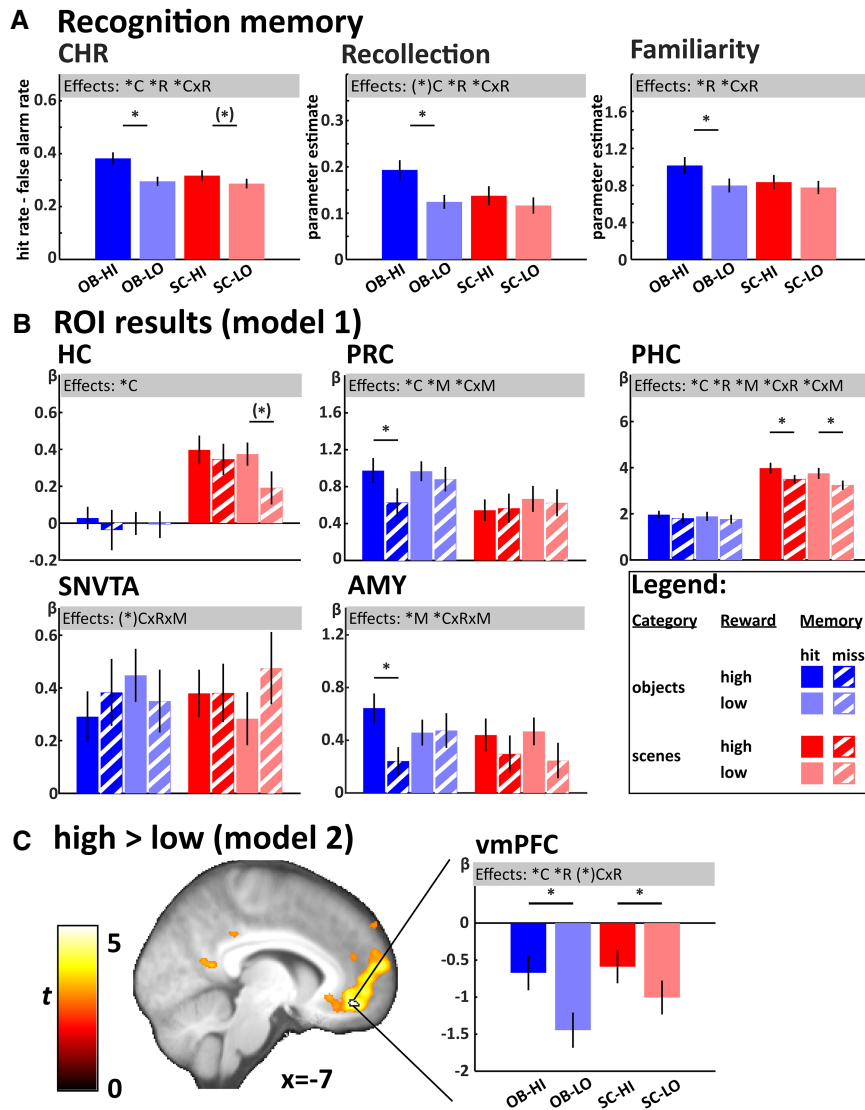


Figure 1. Results overview. (A) Recognition memory results in the memory sample ($n=27$). Gray boxes indicate results from individual two-way repeated measures ANOVAs with the factors category (C) and reward (R). (CHR) Corrected hit rate. (B) Average beta values for each condition of model 1 (memory sample, $n=27$) in each of the five ROIs. Gray boxes indicate results from individual three-way repeated measures ANOVAs with the factors category (C), reward (R), and subsequent memory (M). Paired t -tests (hits vs. misses) were computed for all ROIs and conditions for visualization. (C) Voxel-wise activity for the high > low reward contrast in model 2 (full sample, $n=39$). The statistical map is projected onto the normalized, averaged T1 (display threshold $P < 0.001$ uncorrected, $k \geq 20$ voxels). Black outline indicates vmPFC cluster surviving at $P_{FWE} < 0.05$. Bar plot depicts average beta values within the FWE-corrected vmPFC cluster. The gray box indicates results from a post-hoc two-way repeated measures ANOVA with the factors category (C) and reward (R). (*) $P < 0.05$, [(*)] $P < 0.1$. Error bars indicate SEM.

memory effects in model 1 (see Supplemental Table S2; Supplemental Fig. S3).

fMRI: voxel-wise effects of reward

The previous sections demonstrated clear effects of our reward manipulation on behavioral measures of memory, for objects more so than scenes. The neural effects of reward on memory formation showed a similar asymmetry, with subsequent memory effects in the PRC and AMY for high-reward objects only, and subsequent memory effects in the PHC and AMY for scenes regardless of reward. Against our expectations, however, we did not observe main effects

of reward, or interaction effects of reward with subsequent memory that were independent of category, in either the HC or SNVTA. Therefore, as a control analysis, we tested whether our task succeeded in engaging the reward network using a reduced model with two factors (category and reward; model 2). By disregarding the memory factor, we made use of the increased experimental power of the full sample ($n=39$). Additionally, we used a voxel-wise approach in MNI-normalized data to be able to identify small clusters of activity, which may not be picked up in an ROI analysis.

The high > low reward contrast revealed a cluster of activity that peaked in the vmPFC (MNI coordinates: $-7, 42, -12$, $t_{(38)} = 5.740$, $P_{FWE} = 0.006$) (see Fig. 1C). Clusters in the HC and VS emerged only at an uncorrected threshold of $P < 0.001$ (see Supplemental Table S3). Notably, there was no activity in the SNVTA, even at a relaxed uncorrected threshold of $P < 0.01$.

To assess whether the vmPFC effect was driven by category-specific processing (for example, through an interaction of category and reward), we extracted average beta values within the FWE-corrected vmPFC cluster from each participant's normalized, smoothed beta image (see Fig. 1C) and computed a post-hoc two-way repeated-measures ANOVA with the factors category and reward. This analysis yielded a main effect of reward as expected ($F_{(1,38)} = 23.136$, $P < 0.001$), and additionally a main effect of category (scenes > objects, $F_{(1,38)} = 6.483$, $P = 0.015$), as well as a trend-level interaction (object reward effect > scene reward effect, $F_{(1,38)} = 3.258$, $P = 0.079$). The reward effect (high > low) was significant for both objects ($t_{(38)} = 4.266$, $P < 0.001$) and scenes ($t_{(38)} = 3.158$, $P = 0.003$).

Next, we tested whether whole-brain reward effects differed between objects and scenes. The interaction contrasts (object \times reward interaction [OB-HI > OB-LO] > [SC-HI > SC-LO] and scene \times reward interaction [SC-HI > SC-LO] > [OB-HI > OB-LO]) yielded clusters only at an uncorrected threshold of $P < 0.001$. This included clusters in the vmPFC (object \times

reward interaction) as well as in the HC (scene \times reward interaction) (see Supplemental Table S3).

Last, we ran a conjunction analysis (Nichols et al. 2005) to identify brain regions active in both the OB-HI > OB-LO and SC-HI > SC-LO contrasts. At $P < 0.001$ uncorrected, this analysis again yielded clusters in the vmPFC (see Supplemental Table S3).

Discussion

Summary

The present study's goals were twofold: (1) to investigate how reward modulates memory formation for objects and scenes, and

(2) to investigate whether the documented dichotomy between the PRC and PHC for object and scene memory extends to encoding processes contributing to subsequent recognition memory. Behaviorally, reward enhanced object memory, while evidence for reward enhancement of scene memory was modest. Neural activity in the PRC and PHC predicted subsequent memory for objects and scenes, respectively. Importantly, we report a neural asymmetry mirroring our behavioral findings: Subsequent memory effects for objects were selective for high reward, notably in the AMY, with a similar (albeit nonsignificant) pattern in the PRC. In contrast, subsequent memory effects for scenes in the PHC and AMY did not differ between high and low reward. Finally, main effects of reward were centered on the vmPFC.

Asymmetric effects of reward on behavioral and neural measures of memory

Reward preferentially enhanced object memory. Neurally, subsequent memory effects for objects in the AMY and PRC were pronounced for high-reward objects, whereas subsequent memory effects for scenes in the PHC and AMY were not modulated by reward. We note this effect is unlikely to reflect a general difference between objects and scenes (for example, in salience), since low-reward objects did not differ from low-reward scenes. The clear behavioral bias for high-reward objects is surprising, as previous studies have shown motivational effects on scene memory (Adcock et al. 2006; Bunzeck et al. 2012; Spaniol et al. 2014; Rouhani et al. 2018). Reward effects on memory have been associated with recollection or high-confidence hits (Wittmann et al. 2005, 2011; Adcock et al. 2006), whereas our task yielded a comparatively low memory performance based mainly on familiarity. A more robust reward effect on scenes may emerge with higher proportions of recollection.

Intriguingly, the observed asymmetry fits into an existing framework of memory: PMAT (Ranganath and Ritchey 2012; Ritchey et al. 2015). In PMAT, an anterior-temporal (AT) system, including the PRC and AMY, represents objects and their motivational significance, while a posterior-medial (PM) system, including the PHC, represents (spatial) context. The HC may sharpen and integrate information received from both systems (Ranganath and Ritchey 2012; Ritchey et al. 2015). Indeed, the PRC and AMY have been associated with acquiring stimulus-reward associations (Liu and Richmond 2000; Liu et al. 2000; Rudebeck et al. 2017). The HC has been implicated in reward enhancement of highly confident memory or recollection (Wittmann et al. 2005; Adcock et al. 2006). It is possible that the AT system, including PRC and AMY, suffices for supporting reward enhancement of object memory that is based mainly on familiarity, as reported here. However, scene memory, processed preferably along regions of the PM system, may not benefit from reward unless it reaches the HC's recollection threshold. Indeed, we are not aware of studies showing reward enhancement of low-confident scene memory. These considerations are somewhat speculative and require further research. One prediction would be that the observed asymmetry between reward enhancement of object and scene memory decreases at higher rates of recollection.

Recently, Ritchey et al. (2019) found that another motivational factor, emotion, enhanced item but not context memory. Moreover, the PRC and AMY supported encoding of emotional over neutral items, whereas the PHC and HC supported context encoding for both emotional and neutral items. Item and context processing in the PRC and PHC have been linked to their putative roles in object-related and spatial processing, respectively (Davachi 2006; Eichenbaum et al. 2007), facilitating parallels between Ritchey et al.'s (2019) results and ours. Modulation of item memory, or in our case object memory, by motivational factors may not

require the HC, but instead be carried by the PRC and AMY (note, however, that in this study, the items consisted of scene images, and the context consisted of tasks solved during encoding).

Reward processing in the SNVTA and AMY

Against our hypotheses, we did not observe reward responses in SNVTA, unlike previous work (Wittmann et al. 2005; Adcock et al. 2006; Bunzeck et al. 2012; Wolosin et al. 2012). Some of these studies separated reward cue and encoding stimulus, potentially affecting the dopaminergic response thought to underlie reward enhancement of memory (Shohamy and Adcock 2010). For example, Adcock et al. (2006) presented a cue signaling a reward for successfully encoding an upcoming stimulus and found univariate SNVTA, VS, and HC responses during the cue but not stimulus phases (however, multivariate MTL effects may emerge in both phases) (Wolosin et al. 2013). Other studies presented an encoding stimulus that itself signaled reward via its novelty (Bunzeck et al. 2012) or category (Wittmann et al. 2005), similar to our paradigm. The difference between our and previous findings is therefore unlikely to be due to joint presentation of reward cue and stimulus. Indeed, Shohamy and Adcock (2010) point out that while the timing of stimuli and rewards influences the dopamine response, there are likely several routes through which dopamine enhances memory for stimuli that precede, co-occur with, or succeed the reward.

Much of the research on SNVTA reward signaling comes from reinforcement learning. Activity in the SNVTA and VS, a major target region of SNVTA's dopaminergic projections (Haber and Knutson 2010), varies with reward prediction error (Schultz 1998; O'Doherty et al. 2003; Pessiglione et al. 2006; D'Ardenne et al. 2008; Rolls et al. 2008). Hence, we designed our task to shift the prediction error and putative dopaminergic response to the presentation of the encoding stimulus (Shohamy and Adcock 2010). It is, however, not a learning task, as reward contingencies were explicitly instructed. Diederer et al. (2016) argued that the SNVTA's role in prediction error coding may be pronounced when learning such reward contingencies. While previous studies have shown SNVTA engagement in tasks that did not require such learning (Wittmann et al. 2005; Adcock et al. 2006), future work may investigate whether SNVTA/VS prediction error signaling in a reinforcement learning task covaries with successful episodic memory encoding.

Could other task features explain why we did not find a clear SNVTA effect? The SNVTA has been implicated in reward enhancement of both intentional encoding (with reward contingent on subsequent memory) (Adcock et al. 2006; Wolosin et al. 2012) and incidental encoding such as in our task (Wittmann et al. 2005; Bunzeck et al. 2012; Murty and Adcock 2014). The difference is therefore unlikely to be due to incidental versus intentional encoding. These latter studies also differed in how participants obtained the reward. For example, both Murty and Adcock (2014) and Wittmann et al. (2005) had participants make speeded responses to a secondary task with an adaptive time window, resulting in 65% and 80% reward rate, respectively. In contrast, in our study, participants judged the reward magnitude of the encoding stimulus itself at near-ceiling performance. While not all studies finding SNVTA effects used speeded responses (Bunzeck et al. 2012), SNVTA reward signaling may be related to response vigor (Rigoli et al. 2016) and required effort (Tanaka et al. 2019). Thus, one reason why we did not see the expected SNVTA effects may be the response required from the participants.

While we did not see clear SNVTA effects, our data imply a role of the AMY in reward-enhanced memory. Intriguingly, a recent framework by Murty and Adcock (2017) suggests complementary roles for the SNVTA and AMY in motivated memory formation: During interrogative motivational states, the SNVTA modulates

the HC, forming detailed memories based on recollection. During imperative motivational states, the AMY modulates the MTL cortex, forming sparse memories based on familiarity. The present results—with predominant involvement of the AMY and MTL cortex and largely familiarity-based subsequent recognition—would suggest an imperative motivational state (Murty and Adcock 2017). Murty and Adcock (2017) point out, however, that such states are typically elicited by punishment and, to some extent, by (highly salient) rewards; for example, in addiction. This is not the case here. Furthermore, our behavioral results show highly similar reward effects on both familiarity and recollection. Similarly, exploratory analyses of the recollection-based “remember” trials yielded a reward effect on recollection of source details and suggest involvement of the HC in high-reward scene encoding (these analyses should be interpreted with caution, as they are based on reduced trial and participant numbers) (see Supplemental Fig. S1). Interpreted within the Murty and Adcock (2017) framework, this suggests that both proposed mechanisms may have played a role in the present study. Additionally, we observed a reward-independent subsequent memory effect for scenes in the AMY. The AMY has been implicated in scene encoding, albeit typically modulated by emotion (Kensinger and Schacter 2006; Ritchey et al. 2019). These results indicate that the interplay of category-specific processing, reward, and subsequent memory in the AMY is complex and warrants further research.

Reward processing in the vmPFC

We observed robust reward signals in the vmPFC, a major part of the brain’s reward system (Haber and Knutson 2010). Intriguingly, it also plays a role in memory; namely, in acquiring and using abstract knowledge structures (Hebscher and Gilboa 2016) and representing their value (Paulus et al. 2021). Indeed, in our task, participants matched a stimulus (e.g., a coffee cup with a blue frame) to existing abstract knowledge to determine its value (e.g., “objects surrounded by a blue frame signal high reward”). Moreover, the vmPFC may be necessary for processing configural objects in which a combination of features, but not one feature alone, signals their value (Pelletier and Fellows 2019), as was the case in our study. vmPFC reward effects were significant for both categories; however, the effect may be larger for objects (see Fig. 1C). While the vmPFC has been suggested as a convergence zone of the AT and PM systems (Ranganath and Ritchey 2012; Ritchey et al. 2015), anatomical connectivity between that region and the MTL cortex varies along the anterior–posterior MTL axis (Kondo et al. 2005; Price 2007; Kondo and Witter 2014) and may be particularly pronounced for the anterior MTL cortex (the PRC and EC) (Eichenbaum 2017; but see Kahn et al. 2008). Therefore, a query for future work is whether vmPFC responses could bias reward-related object encoding by modulating one MTL pathway over the other.

Category-specific incidental memory encoding in the MTL cortex

Across reward conditions, we observed a dissociation of category-specific incidental memory encoding in the PRC and PHC, with object encoding in the PRC and scene encoding in the PHC. Category specificity in the MTL has been demonstrated in a number of imaging studies for processes including perception (Litman et al. 2009; Liang et al. 2013; Berron et al. 2018), associative encoding (Awipi and Davachi 2008; Staresina et al. 2011), associative retrieval (Staresina et al. 2012, 2013; Mack and Preston 2016; Schultz et al. 2019, 2022), short-term memory reactivation (Schultz et al. 2012), and recognition-based retrieval (Martin et al. 2013; Kafkas et al. 2017). However, to our knowledge, our study is the first to

demonstrate a double dissociation between the PRC and PHC for encoding processes contributing to subsequent recognition memory for objects and scenes, filling an important gap in the literature and supporting a model of MTL function that draws on anatomical connectivity to predict functional specialization (Davachi 2006; Eichenbaum et al. 2007).

While scene-specific subsequent recognition memory effects have been observed in the PHC and larger parahippocampal place area (Prince et al. 2009; Preston et al. 2010), the same cannot be said for object-specific subsequent recognition memory effects in the PRC. Preston et al. (2010) observed subsequent memory effects for both faces and scenes in the PRC. In contrast, the PRC in our study did not show a subsequent memory effect for scenes at all. Unlike our study, Preston et al. (2010) assessed immediate rather than next-day recognition memory, and participants were aware of the upcoming recognition test. As discussed above, on a descriptive level, our object-encoding effect in the PRC is specific to high-reward objects. It is possible that while incidental encoding does not engage the PRC in a category-specific fashion, adding a motivational factor such as reward does.

While our main results suggest category specificity (i.e., subsequent memory effects for objects but not scenes in the PRC, and for scenes but not objects in the PHC), category processing in the PRC and PHC is unlikely to be exclusive. Subsequent memory effects have been noted for faces and scenes in the PRC (Preston et al. 2010), for scenes in both the PRC/EC and PHC (Adcock et al. 2006), and for object pairs in the PHC (Wolosin et al. 2012, 2013). Even in the present study, exploratory analyses of the remember-only trials (see Supplemental Fig. S1) suggest an additional subsequent memory effect for high-reward objects in the PHC. Relative category preference may stem not only from overlap in the stimuli (e.g., scenes usually contain objects, and objects usually have a spatial or configurational aspect) and high interconnectedness between the PRC and PHC (Suzuki and Amaral 1994a; Lavenex and Amaral 2000), but also from category-independent processes. For example, it is possible that intentional encoding processes in Preston et al. (2010) led to additional involvement of the PRC in scene encoding. Importantly, even if memory processes are held constant, category preference emerges (Awipi and Davachi 2008; Staresina et al. 2011, 2012, 2013; Martin et al. 2013; Schultz et al. 2019, 2022). However, it has been suggested that object and spatial processing map preferentially onto distinct processes: item memory/familiarity in the PRC, and associative memory/recollection in the PHC and HC (Davachi 2006; Eichenbaum et al. 2007). Indeed, the PRC and PHC also distinguish between item and context recall even when the stimulus material is held constant (Wang et al. 2013), and experimental manipulations may have dissociable effects on different memory processes (Wittmann et al. 2005, 2011; McCullough et al. 2015; Madan et al. 2017; Ritchey et al. 2019). Thus, process dissociations may have additional predictive value for MTL function that go beyond a distinction based on stimulus categories.

Category specificity and category independence in the HC

The HC showed a robust effect of scene viewing compared with object viewing. While some accounts see the HC’s role in memory as category-independent (Davachi 2006; Eichenbaum et al. 2007), others emphasize its role in spatial (Moser et al. 2008; Hartley et al. 2014) and scene (Maguire and Mullally 2013) processing. Moreover, while we observed a pronounced scene viewing effect in the HC, an earlier study—using a similar stimulus set, albeit a different (intentional and associative) encoding task—did not (Schultz et al. 2019). Targeted investigations of HC subfields may further specify the circumstances in which HC responses are category-specific or category-independent (Dalton et al. 2018).

We also did not observe overall effects of subsequent memory in the HC. The HC has been implicated in recollective or highly confident recognition memory (Wittmann et al. 2005; Adcock et al. 2006; Eichenbaum et al. 2007). Memory performance in the present study was overall low, which may explain why neural encoding processes were mainly observed in the MTL cortex, thought to support familiarity (Eichenbaum et al. 2007; Martin et al. 2013), rather than the HC. Notably, the response pattern in HC (see Fig. 1B) suggests a subsequent memory effect selective for low-reward scenes, potentially centered on the anterior HC (see Supplemental Fig. S2). In contrast, an exploratory analysis of the “remember”-only trials suggested a subsequent memory effect in the HC selective for high-reward scenes (see Supplemental Fig. S1), in line with the findings by, for example, Adcock et al. (2006) and Wolosin et al. (2012). In sum, our results are not conclusive with regard to the role of the HC in reward enhancement of memory.

Future directions

The fate of a memory trace is not solely determined by neural processing during encoding. For example, reward during encoding may enhance postencoding consolidation processes by biasing recently encoded memories for offline replay (Kumaran et al. 2016). Similarly, reward associations acquired during encoding modulate brain activity during retrieval (Wolosin et al. 2012; Elward et al. 2015). Thus, the observed behavioral effects of reward on object memory may have been driven in part by neural processing outside the time window observed in the present study, which may be addressed in future work.

Conclusions

In sum, we present novel evidence that reward preferably modulates object rather than scene encoding, evident in behavioral measures and anterior temporal lobe signaling. In addition, we demonstrate a double dissociation between the anterior and posterior MTL cortices for incidental memory encoding, leading to successful recognition of objects and scenes, respectively. A potential limitation of our study lies in the comparatively low memory performance, which was mainly based on familiarity rather than recollection. Future work may further elucidate the neural mechanisms underlying the distinct effects of reward on the encoding of different stimulus categories.

Materials and Methods

Participants

A total of 39 participants (“full sample,” 25 female, mean age 24.2 yr, range 18–32) took part in the study. All were right-handed, had normal or corrected-to-normal vision, and were native speakers of German. A subsample of 27 participants (“memory sample,” 19 female, mean age 24.6 yr, range 19–32) was selected for memory-based analyses (model 1) based on their memory performance (corrected hit rate [CHR] > 0.083 in each of the four conditions, see below; this threshold was chosen as a compromise between memory performance and experimental power). Additional non-memory-based analyses (model 2) were carried out on the full sample. All participants gave written informed consent in a manner approved by the local ethics committee

and received monetary reimbursement (€8 per hour plus up to €5 bonus during the incidental encoding task). Thirty-three fMRI data sets were complete, contributing 240 trials each; six suffered partial data loss due to equipment malfunction, contributing 200–238 trials each.

Stimuli and procedure

We obtained 360 color photographs of objects and scenes (180 each) from established databases (Brady et al. 2008; Konkle et al. 2010a,b) and an internet search. Of these, 240 (120 objects and 120 scenes) served as targets in the incidental encoding task; the others served as distractors in the surprise recognition task. Assignment of images to targets and distractors was randomized for each participant. An additional eight photographs (four objects and four scenes) were obtained from the same sources and used during training before the incidental encoding task. Each image was sized 256 × 256 pixels. All tasks were programmed using Presentation software (version 18.2, Neurobehavioral Systems, Inc., <https://www.neurobs.com>). The scanned encoding task was projected onto a mirror mounted on the head coil; responses were collected using an MRI-compatible button box. The behavioral recognition task was presented on a laptop.

Day 1: incidental encoding task (fMRI)

The incidental encoding task (see Fig. 2A) fully crossed stimulus category (objects and scenes) and anticipated reward magnitude (high and low), resulting in the following experimental conditions: object-high (OB-HI), object-low (OB-LO), scene-high (SC-HI), and scene-low (SC-LO). The task was presented in six runs of 40 trials each (240 trials total). Trials were pseudorandomized so that each run contained equal trial numbers of each condition, and no more than three trials belonging to the same level of each factor (category and reward) appeared in a row. Each trial consisted of a cue, choice, and outcome phase (see Fig. 2A for example trials for each condition). During the cue phase (2 sec), an image (object or scene) appeared with a yellow or blue frame. Importantly, the combination of image category and frame color coded reward magnitude (e.g., object-yellow or scene-blue indicated high reward, while object-blue or scene-yellow indicated low reward). Category–frame combinations were explicitly instructed at the beginning of each run and alternated over runs, with the order counterbalanced over participants. The cue phase was followed by a variable fixation (1–5 sec, drawn randomly from a uniform

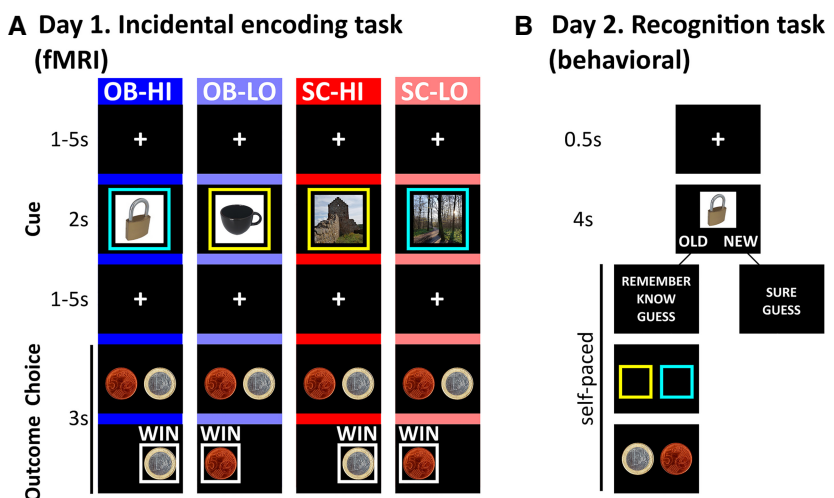


Figure 2. Experimental paradigm. (A) Day 1: incidental encoding task. (B) Day 2: recognition task. Note that text options (e.g., remember—know—guess) were arranged horizontally in the experiment. See the text for details. (OB) Objects, (SC) scenes, (HI) high reward, (LO) low reward. Example stimuli have been replaced with similar photographs due to copyright.

distribution). During the following choice phase, two coins were presented, respectively, on the left and right side of the screen and participants indicated whether they anticipated a high (€1) or low (€0.05) reward. Response sides were assigned randomly. Upon button press, the chosen coin was outlined with a white frame for 0.5 sec or until 2 sec after choice onset, whichever was shorter. In the outcome phase, only the chosen coin (€1 or €0.05) remained on the screen and the word GEWINN (“Win”) appeared if the participant had chosen the correct reward magnitude. For incorrect choices, the coin would be crossed out, and the word NICHTS (“nothing”) appeared. If no button was pressed, the coin would also be crossed out, and the words ZU LANGSAM (“too slow”) appeared. The outcome phase lasted 1 sec or until 3 sec after choice onset, whichever was longer. Trials were offset by a variable fixation interval (1–5 sec, drawn randomly from a uniform distribution).

Note that we varied reward magnitude (high vs. low), rather than presence versus absence of reward. Hence, the task was designed to produce ceiling performance to ensure that participants received the high or low reward in the majority of trials. Trials in which participants did not gain the reward were excluded from further analysis. Additionally, we presented the image and frame simultaneously to cue reward magnitude, rather than using a prestimulus reward cue, and reward probability was 100%, provided that participants correctly indicated the reward magnitude during the choice phase. These measures were taken to ensure that participants paid attention to the image and to shift the assumed dopamine response from the reward outcome to the reward cue presentation (image plus frame) (Shohamy and Adcock 2010). A fraction of the winnings (up to €5, with high-reward stimuli 20× more valuable than low-reward stimuli) was paid out directly after the fMRI session on day 1. This was to reduce reward discounting due to delayed gratification (Peters and Büchel 2011).

Day 2: recognition task (behavioral)

The next day, participants returned to the laboratory to complete a surprise recognition test (see Fig. 2B). All 120 objects and 120 scenes from the fMRI task (targets) were presented again without the colored frames, as well as 60 novel objects and 60 novel scenes (distractors). Stimuli were presented in six runs. Stimulus order was pseudorandomized such that each run contained equal trial numbers of each condition and no more than three stimuli belonging to the same level of each factor (category and reward), and no more than three distractors appeared in a row. For each image, participants indicated whether the image was NEU (“new”) or ALT (“old”). “New” judgments were followed by a choice between SICHER (“sure”) and GERATEN (“guess”). “Old” judgments were followed by a choice between ERINNERT (“remember”), BEKANNT (“know”), or GERATEN (“guess”). This is an established procedure to distinguish between two processes thought to underlie recognition memory: recollection and familiarity (Tulving 1985; Yonelinas et al. 2010). Participants were instructed to only indicate “remember” if they had a vivid recollection of the image, including recall of contextual information. This was followed by two source memory tasks, consisting of forced-choice screens for the frame color and reward magnitude. All judgments were self-paced except the initial “old”/“new” judgment (4 sec).

Conditions of interest

In the encoding task, we manipulated stimulus category (OB [object] and SC [scene]), and reward (HI [high] or LO [low]), resulting in four combinations: OB-HI, OB-LO, SC-HI, and SC-LO. The “old”/“new” choices from the day 2 recognition phase were then used to back-sort the trials from the day 1 encoding phase into the following conditions of interest: OB-HI-H (object–high reward–hit), OB-HI-M (object–high reward–miss), OB-LO-H (object–low reward–hit), OB-LO-M (object–low reward–miss), SC-HI-H (scene–high reward–hit), SC-HI-M (scene–high reward–miss), SC-LO-H (scene–low reward–hit), and SC-LO-M (scene–low reward–miss).

Behavioral analyses

For the encoding task, we calculated accuracy (proportion of correct responses) separately for each encoding condition (OB-HI, OB-LO, SC-HI, and SC-LO). Accuracies were then submitted to a two-way repeated measures ANOVA with the factors category and reward. For the recognition task, we calculated corrected hit rate (CHR) as the hit rate (proportion of “old” responses to targets) minus the false alarm rate (proportion of “old” responses to distractors), separately for object and scene distractors). Additionally, from the distributions of “remember” and “know” responses, we calculated estimates for recollection and familiarity using the formula described in Yonelinas and Jacoby (1995). CHR, recollection, and familiarity were calculated separately for each encoding condition (OB-HI, OB-LO, SC-HI, and SC-LO) and submitted to two-way repeated measures ANOVAs with the factors category and reward.

MRI acquisition

The study was scanned on a Siemens Tim Trio 3T MRI scanner using a 32-channel head coil. First, a high-resolution T1-weighted structural image was scanned (MPRAGE, 1-mm isotropic voxels). Next, six functional runs were acquired using a T2*-weighted gradient-echo, echo-planar pulse sequence (40 interleaved slices, 1.5 mm × 1.5 mm in-plane resolution, 2-mm slice thickness with 20% distance factor, TR = 1800 msec, TE = 30 msec, multiband factor = 2, PAT factor [GRAPPA] = 2, 260 volumes per run). Slices were oriented in parallel to the AC–PC line and adjusted to optimize PFC coverage, with the field of view covering nearly the whole brain except for the very superior frontal and parietal cortex. The first five images of each run were discarded to allow for magnetic field stabilization. Finally, a 3D magnetization transfer (MT) FLASH structural image was acquired (1-mm isotropic voxels).

fMRI preprocessing and analysis

Strategy

Our main analyses were carried out within bilateral participant-specific regions of interest (ROIs), including the MTL subregions HC, PRC, and PHC, and additionally the AMY and SNVTA (see Fig. 3). The MTL and AMY ROIs were manually segmented on each participant’s T1 image using established landmarks (Insausti et al. 1998; Pruessner et al. 2000, 2002). As object and scene selectivity changes gradually along the MTL cortex axis (Litman et al. 2009; Liang et al. 2013), to optimize category selectivity we discarded the putative transition zone (posterior PRC and anterior PHC) in line with previous studies (Staresina et al. 2011, 2012, 2013; Schultz et al. 2019). The SNVTA was manually segmented on each participant’s MT image as described in Bunzeck and Düzel (2006). Control analyses were carried out on a voxel-wise level in Montreal Neurological Institute (MNI) space.

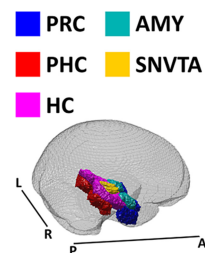


Figure 3. ROIs. Single-participant regions of interest were MNI-normalized, averaged over the full sample ($n = 39$), and thresholded at 0.5. Here they are visualized within the standard SPM12 brain mask (mask_ICV.nii). (PRC) Perirhinal cortex, (PHC) parahippocampal cortex, (HC) hippocampus, (AMY) amygdala, (SNVTA) substantia nigra/ventral tegmental area, (A) anterior, (P) posterior, (R) right, (L) left.

fMRI analysis pipeline

Functional runs were corrected for differences in slice acquisition time, and then realigned and unwarped to correct for movement and movement-related distortions using SPM12 (Wellcome Trust Center for Neuroimaging, <https://www.fil.ion.ucl.ac.uk/spm>). The T1 image was coregistered to the mean functional volume using SPM12 followed by boundary-based registration (FSL `epi_reg`). The MT image was then coregistered to the T1 using SPM12. First-level statistical analyses (see below for details) were carried out on the nonnormalized, unsmoothed data. For the ROI analyses, ROIs were resampled to functional space, and first-level beta values were averaged across all voxels of each ROI. For the voxel-wise analyses, T1 images were segmented into gray matter, white matter, and cerebrospinal fluid using SPM12. Deformation fields from this step were then used for MNI normalization of the first-level beta images. The normalized beta images were resampled to a 1-mm isotropic voxel size and smoothed with a Gaussian kernel (6-mm full width at half maximum).

fMRI statistics

First-level general linear models were set up in SPM12. The six functional runs were concatenated. For our main analyses (model 1), the following conditions of interest were modeled: OB-HI-H, OB-HI-M, OB-LO-H, OB-LO-M, SC-HI-H, SC-HI-M, SC-LO-H, and SC-LO-M. Conditions were modeled as impulse regressors using a canonical hemodynamic response function (HRF). Each trial phase (cue, choice, and outcome) was modeled separately, and subsequent analyses were focused on the cue phase. Additional regressors of no interest modeled error trials separately for object and scene trials. Error trials were defined as incorrect or no response during the incidental encoding task and/or no response during the old/new choice of the recognition task. Model 2 was set up identically, except the conditions of interest did not include the memory factor (hence, OB-HI, OB-LO, SC-HI, and SC-LO). Models included a high-pass filter (128s), an autoregressive model [AR(1)], and run constants. For the ROI analyses (model 1), beta images were averaged across voxels of each participant's ROIs and submitted to a group-level four-way repeated measures ANOVA with the factors region, category, reward, and subsequent memory. Where appropriate, Greenhouse-Geisser correction was applied. Follow-up analyses were then carried out within each ROI. For the voxel-wise analyses (model 2), normalized, smoothed beta maps were submitted to a second-level random effects analysis (flexible factorial as implemented in SPM12) that included the factors category and reward as well as a subject factor. The resulting brain activation maps were corrected for multiple comparisons using peak-level family-wise error correction (FWE) across the whole brain.

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