SPECIAL ISSUE/REWARD SYSTEMS, COGNITION,AND EMOTION

CrossMark

Functional connectivity between memory and reward centers across task and rest track memory sensitivity to reward

Lea E. Frank[1] · Alison R. Preston[2] · Dagmar Zeithamova[1]

Abstract

External motivation, such as a promise of future monetary reward for remembering an event, can affect which events are remembered. Reward-based memory modulation is thought to result from encoding and post-encoding interactions between dopaminergic midbrain, signaling reward, and hippocampus and parahippocampal cortex, supporting episodic memory. We asked whether hippocampal and parahippocampal interactions with other reward-related regions are related to reward modulation of memory and whether such relationships are stable over time. Individuals' memory sensitivity to reward was measured using a monetary incentive encoding task in which a cue indicated potential monetary reward (penny, dime, or dollar) for remembering an upcoming object pair. Functional connectivity between memory and reward regions was measured before, during, and following the task. Reward-related regions of interest were generated using a meta-analysis of existing studies on reward and included ventral striatum, medial and orbital prefrontal cortices and anterior cingulate cortex, in addition to midbrain. The results showed that connectivity between memory and reward regions tracked individual differences in reward modulation of memory, irrespective of when connectivity was measured. Connectivity patterns of anterior cingulate, orbitofrontal cortex, and ventral striatum covaried together and tracked behavior most strongly. These findings implicate a broader set of reward regions in reward modulation of memory than considered previously and provide new evidence that stable connectivity patterns between memory and reward centers relate to individual differences in how reward impacts memory.

Keywords Episodic memory · Functional connectivity · Hippocampus · Motivation · Reward · Prefrontal cortex

Why are some events remembered and others forgotten? Reward-based motivation is one factor that impacts which events are remembered. The modulation of memory by rewards is thought to result from reward-related activation of the dopaminergic midbrain and the projection of dopamine into the hippocampus, which facilitates long-term potentiation and memory formation (Lisman & Grace, 2005; Lisman, Grace, & Duzel, 2011; Shohamy & Adcock, 2010). Consistent with this model, several functional MRI studies have documented increased activation in the midbrain and ventral striatum, accompanied by univariate and multivariate signals reflecting reward in the hippocampus and parahippocampal cortex (PHC) within the medial temporal lobe (Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006; Gruber, Ritchey, Wang, Doss, & Ranganath, 2016; Wittmann et al., 2005; Wolosin, Zeithamova, & Preston, 2012, 2013). A common finding in these studies is that individuals differ in the degree to which their memory is affected by extrinsic rewards (Adcock et al., 2006; Gruber et al., 2016; Wolosin et al., 2012, 2013).

Individual differences in memory sensitivity to reward have been related to both phasic and tonic interactions between the midbrain and medial temporal lobe (Shohamy & Adcock, 2010). Adcock et al. (2006) first found that task-related activation in the hippocampus, PHC, midbrain, and ventral striatum were correlated participants. Wolosin et al. (2012) showed background hippocampal-midbrain interactions across both encoding and retrieval phases track memory sensitivity to reward. Other studies focused on learning-induced connectivity increases, relating them to reward-motivated memory (Gruber et al., 2016; Murty, Tompary, Adcock, & Davachi, 2017), although hippocampal-midbrain

✉ Dagmar Zeithamova
  dasa@uoregon.edu

1 Department of Psychology, University of Oregon, 1227 University Street, Eugene, OR 97403, USA

2 Center for Learning and Memory and Department of Psychology, The University of Texas at Austin, Austin, TX 78712, USA

Springer

interactions may relate to associative memory in general (Duncan, Tompary, & Davachi, 2014; Tompary, Duncan, & Davachi, 2015).

Across many memory studies, the emphasis has been on connectivity during task performance or connectivity changes after learning as primary predictors of behavior (Gruber et al., 2016; Murty et al., 2017; Tambini, Ketz, & Davachi, 2010; Tompary et al., 2015). In contrast, other fields have focused on resting connectivity patterns, given that individual differences of intrinsic connectivity can remain relatively stable across time and tasks (Finn et al., 2015; Gratton et al., 2018), predicting individual differences in cognition (Finn et al., 2015; Gerraty, Davidow, Wimmer, Kahn, & Shohamy, 2014; Poole et al., 2016; Wang et al., 2010). Therefore, we wanted to bridge these approaches and test whether there are stable interactions between memory and reward regions that track individual differences in memory sensitivity to reward, irrespective of when those interactions are measured. For example, even in the absence of a task, the strength of connectivity between hippocampus, midbrain, and ventral striatum varies across individuals (Kahn & Shohamy, 2013). Because these regions are involved in memory and reward processes, these task-independent interactions may relate to individual differences in memory sensitivity to reward. However, the idea of an individual's connectivity "fingerprint"—used in a broad sense referring to connectivity patterns differentiating groups and tracking performance (Gratton et al., 2018; Wang et al., 2010) rather than identifying specific individuals (Finn et al., 2015)—has not yet been tested in the area of reward modulation of memory.

Theoretical perspectives, particularly the Lisman and Grace (2005) model, have emphasized the role of the dopaminergic midbrain in motivated learning. Influenced by this model, neuroimaging studies on memory sensitivity to reward have typically focused on the midbrain as the primary reward region of interest (Adcock et al., 2006; Gruber et al., 2016; Wittmann et al., 2005; Wolosin et al., 2012). However, other reward-related regions are likely to contribute to motivational effects on memory. The ventral striatum is believed to play a central role integrating signals between the hippocampus and midbrain (Lisman & Grace, 2005; Miendlarzewska, Bavelier, & Schwartz, 2016), is recruited during motivational encoding (Adcock et al., 2006; Wittmann et al., 2005), and has been shown to interact with the hippocampus both during rest (Kahn & Shohamy, 2013) and task performance (Adcock et al., 2006; Camara, Rodriguez-Fornells, & Münte, 2009; Kafkas & Montaldi, 2015). Prefrontal regions, including the orbitofrontal cortex (OFC) and medial prefrontal cortex (MPFC), also interact with hippocampus and PHC (Blessing, Beissner, Schumann, Brünner, & Bär, 2016; Gerraty et al., 2014; Murty, LaBar, & Adcock, 2016) and have been implicated in various reward-related processes (Amiez, Joseph, & Procyk, 2006; Elliott, Agnew, & Deakin, 2008;

Kable & Glimcher, 2007). However, because of the theoretical emphasis on midbrain, and to a lesser degree striatum, it is unknown whether other reward-related regions also contribute to reward modulation of memory.

The current study had two main goals. First, we sought to determine the role of a broader network of reward-related regions in mediating reward modulation of memory. Reward-related regions of interest were independently derived based on their involvement in reward processing using an automated meta-analysis tool Neurosynth (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011), irrespective of their prior implication in reward modulation of memory. Second, we aimed to determine to what extent individual differences in memory sensitivity to reward relate to individual differences in connectivity between memory and reward centers and whether such a relationship may exist irrespective of when connectivity is measured. To evaluate the stability of connectivity patterns and their relationship to behavior, interactions between hippocampus and PHC with a network of reward-related regions were measured using functional MRI during a monetary incentive encoding task (Adcock et al., 2006), as well as during rest scans before and after the task. The pattern of connectivity for each participant was related to their memory sensitivity to reward, defined as memory advantage for high-value trials, using analysis of variance and machine-learning approaches. A separate report from this data set, focusing on hippocampal and PHC task-related activation patterns and how they represent reward, has been published previously (Zeithamova, Gelman, Frank, & Preston, 2018).

Materials and methods

Participants

Thirty-four healthy, English speaking volunteers enrolled in this study. Data from nine participants were excluded for excessive head motion during task scans (framewise displacement >1 mm in at least 50 time points in more than 1 run; 4 participants), scanning interruptions (3 participants), or missing data (2 participants). An additional participant was excluded due to excessive head motion during a rest scan (>50% of time points removed during scrubbing). The remaining 24 subjects (18 females, ages 18-31, mean age = 22) were included in the connectivity analyses. Subjects received $40 for participation and up to $55.50 bonus for their memory performance. The study was approved by the Institutional Review Board of The University of Texas at Austin, and all participants provided a written consent. A separate sample of 20 participants (5 females, ages 18-24 years, mean age 19 years) completed the same task but were not scanned.

Behavioral procedures

Following the consent procedure, participants were instructed on the task and completed five practice trials. Next, they were screened for MRI, changed into scrubs, and were positioned into an MRI magnet. The scanning session started with the acquisition of anatomical scans, followed by functional scans. Participants completed a pre-encoding rest scan (6 minutes), a motivated encoding task across five event-related runs (9 minutes each), and a post-encoding rest scan (6 mins), with 1-2 minutes between all scans (Fig. 1a). During rest scans, participants were instructed to keep their eyes open, with a blank screen in front of them. During the motivated encoding task, participants were instructed to intentionally encode 150 pairs of common objects, each preceded by a cue (in pictorial or word form), indicating a reward value (penny, dime, or dollar) that they may earn if they remembered the object pair in a later memory test (Fig. 1b). The object pairs were drawn from a set of 300 color photographs of objects and randomly assigned to one of the six reward-cue conditions, resulting in 25 pairs per condition. Participants were informed that they would receive a cash bonus indicated by the reward cue for correctly recalling the associations in a cued-recall task that immediately followed the scanning session. Trials from all conditions were presented in a randomized order, with a balanced number of presentations in each of the five encoding runs. A self-paced cued recall test was completed following the scanning session, approximately 20-30 minutes after the post-encoding rest. During each test trial, participants were shown the left object of each pair and asked to name aloud the associated

object, followed by a source memory test during which participants selected the reward cue that preceded that object (Fig. 1c). Participants were not informed that they would be tested on the cue identity prior to the test. Source memory for cue identity was at chance in the fMRI sample (Zeithamova et al., 2018) and is not considered further in this report.

For each participant, the mean proportion of correctly recalled associations following each of the six possible cues was computed. A 2 (form: picture, word) × 3 (value: penny, dime, dollar) repeated measures ANOVA examined the within-subjects effect of reward value and form on memory. For significant effects, follow-up pairwise comparisons were conducted to determine the differences between the mean accuracies of each condition. The behavioral data were used to index individual differences in reward modulation of memory. Because the behavioral effect of reward was found to be U-shaped in the fMRI sample, we used the difference between dollar and dime trial accuracy as a measure of memory sensitivity to reward. We refer to this score as the *behavioral reward modulation* (BRM) score. Additionally, a median split of BRM scores sorted participants into two groups: modulators (those who demonstrated memory sensitivity to reward), and nonmodulators (those whose memory scores were insensitive to reward). A confirmatory analysis of the reward effect on memory was performed within each group to verify that "modulators" indeed showed a memory advantage for dollar trials while "nonmodulators" did not. We refer to this dichotomized measure of memory sensitivity to reward as a *modulator status*.
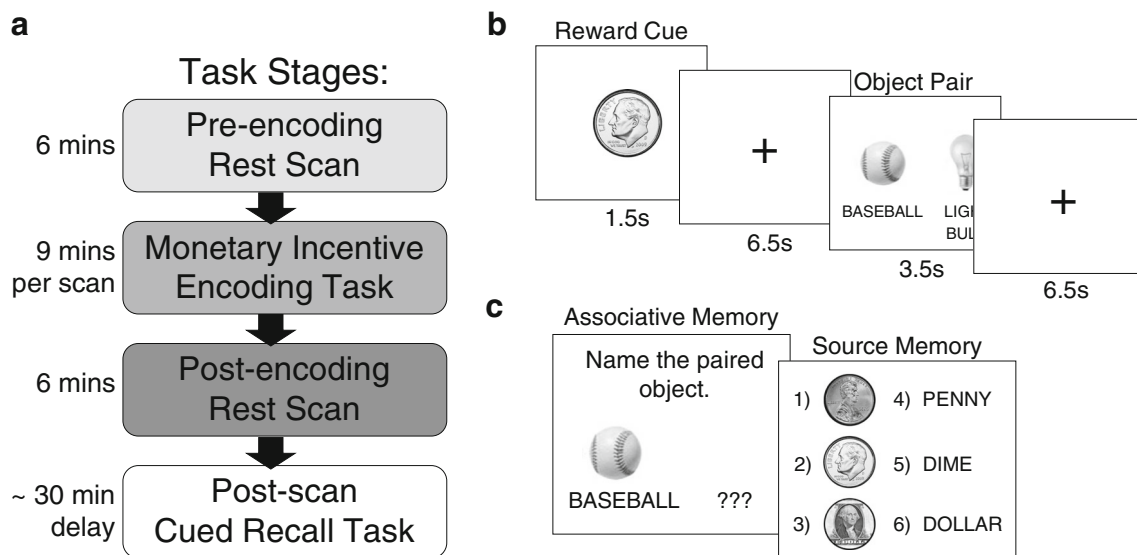

Fig. 1. Behavioral procedures. **a** The task consisted of three scanning stages: the pre-encoding rest scan, the monetary incentive encoding task, and the post-encoding rest scan. The final stage consisted of a cued recall task that was conducted outside of the scanner. **b** Participants performed a modified monetary incentive task. They were asked to intentionally encode pairs of common objects. Preceding each object pair was a reward

cue that indicated how much money the participant would earn for correctly remembering the object pair. **c** In a post-scan cued recall task, participants had to name the object previously paired with the one presented. A surprise source memory task for the associated reward cue followed each trial

fMRI acquisition

Functional and structural MR images were collected at the Imaging Research Center at the University of Austin at Texas using a 3T Siemens Skyra MRI scanner. Functional images were collected in 72 oblique axial slices, approximately 20 degrees from the AC-PC line, using echo-planar imaging sequences with multiband acceleration factor = 3, GRAPPA factor = 2, TR = 2,000 ms, TE = 31 ms, flip angle = 73°, 128 × 128 × 72 matrix resulting in 1.7-mm isotropic voxels. Using the same parameters, two 6-minute resting-state fMRI scans were conducted, one preceding and one following the encoding task. A T1weighted high-resolution MPRAGE anatomical image (256 × 256 × 192 matrix, 1-mm isotropic voxels) was collected. An additional T2-weighted image was collected in an oblique coronal plane perpendicular to the hippocampal axis (TR = 13,150 ms, TE = 82 ms, 512 × 60 × 512 matrix, 0.4- × 0.4-mm in-plane resolution with 1.5-mm slices, no gap).

Regions of interest

Because prior studies on motivated encoding have primarily focused on midbrain, little is known about how other reward-related regions may affect memory sensitivity to reward. Our goal was to include a wider reward-related network in the current investigation, irrespective of whether they have been previously implicated in reward modulation of memory. To obtain ROIs related to reward processing, a meta-analysis of 671 studies including the term "reward" was collected from the Neurosynth database (http://neurosynth.org). We used the "reverse inference" map (currently referred to as the "association test"), which displays regions that preferentially activate in studies that include the term "reward" compared with studies that do not include the term "reward" and as such is considered diagnostic of the term in question (Yarkoni et al., 2011). Because the default Neurosynth threshold (FDR $p < 0.01$) yielded large clusters with multiple peaks in anatomically distinct regions, we further thresholded the maps with a voxel-wise threshold of Z = 5.3 to obtain clusters that did not extend across multiple anatomical regions. This meta-analysis resulted in five reward-related ROIs that centered on the anterior cingulate cortex (ACC), midbrain, medial prefrontal cortex (MPFC), orbitofrontal cortex (OFC), and ventral striatum (VS). Clusters centered on the midbrain and VS were disproportionately larger than the prefrontal ROIs and extended beyond the anatomical boundaries of their respective regions, thus these clusters were further reduced to the top 500 voxels. The localization of the resulting five reward-related ROIs in the standard space is presented in Fig. 2a. The reward-related ROIs were reverse transformed from standard space to native space of each participant using FLIRT, a part of FSL (http://www.fmrib.ox.ac.uk/fsl). Finally, the reward ROIs were

resampled to the functional space of the participant to serve as masks for extracting timeseries.

Given the number of reward-related regions, only hippocampus and PHC were selected as memory regions of interest to limit the total number of connections considered. Hippocampus and PHC were selected as our *a priori* memory ROIs, because they have been consistently implicated in studies of reward effects on memory (Gruber et al., 2016; Wolosin et al., 2012, 2013). To obtain unbiased ROIs, we defined hippocampus and PHC anatomically in each participant's native space. We did not use a functional definition (e.g., Neurosynth) as it was not apparent whether standard memory voxels in these regions must be also most relevant for memory modulation by reward. However, the Neurosynth "memory" maps do cover essentially the whole anatomical hippocampus and PHC and would thus yield the same results. Anatomical ROIs were obtained by cortical parcellation and subcortical segmentation of the T1 anatomical scan via Freesurfer (https://surfer.nmr.mgh.harvard.edu). The T1 anatomical scan was then coregistered to the first functional scan using Advanced Normalisation Tools (ANTS, http://picsl.upenn.edu/software/ants/), and the coregistration parameters were applied to the Freesurfer segmentations. Finally, the participant-specific, Freesurfer-defined hippocampus and PHC were transformed into the space of their functional scans to be used as masks for extracting hippocampal and PHC timeseries. Hippocampus and PHC ROIs are presented for an example subject in Fig. 2b.

Deriving functional connectivity measures

Preprocessing was conducted using tools from FSL version 5.0 and ANTS. The functional and anatomical images were brain extracted using BET. Functional images were motion corrected within each run using FLIRT from FSL, realigned across runs to the first functional image using ANTS, and high-pass filtered (128-s cutoff). Functional connectivity was measured during the pre-encoding rest scan, the five encoding scans, and the post-encoding rest scan using similar processing procedures. As connectivity measures may be affected by noise in the BOLD signal evoked by motion and physiological processes (Murphy, Birn, & Bandettini, 2013; Power, Barnes, Snyder, Schlaggar, & Petersen, 2012), we followed the preprocessing procedures outlined by Power et al. (2012) to remove noise-related signal fluctuations. First, time courses were extracted for cerebrospinal fluid (CSF), white matter (WM), and the whole brain, because signal changes in these regions provide a good proxy to signal changes driven by motion and other confounds. The six realignment motion parameters, framewise displacement (FD), and global signal change (DVARS) also were extracted. We then created a "scrubbing" mask using the time series for FD and DVARS. Time points that exceeded either threshold (FD > 0.5 mm or

a

| Anterior Cingulate Cortex (ACC) | Midbrain (MID) | Medial Prefrontal Cortex (mPFC) | Orbitofrontal Cortex (OFC) | Ventral Striatum (VS) |

b

■ Hippocampus (HIP)
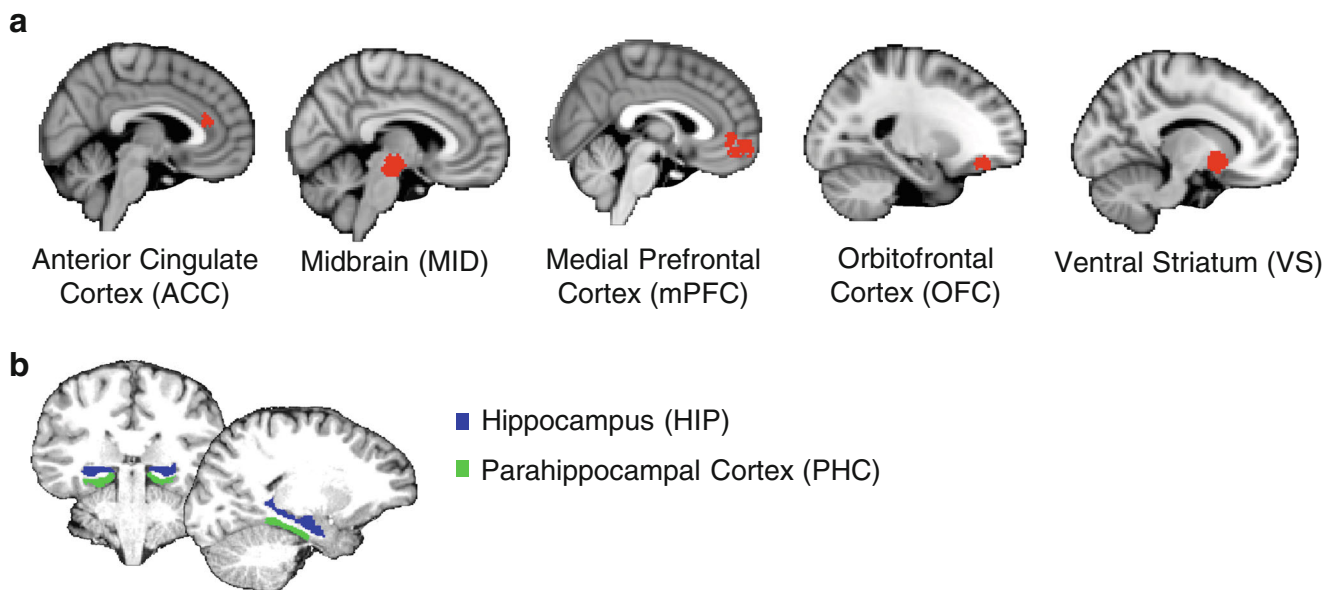
■ Parahippocampal Cortex (PHC)

Fig. 2. Regions of interest. **a** Localization of five reward-related ROIs extracted from Neurosynth. **b** Memory ROIs were anatomically defined hippocampus and PHC, shown on an example subject in native space

DVARS > 0.5%) were marked for removal, as was one time point before and two time points after (Power et al., 2012). Additionally, the first two time points in each scan were removed. The scrubbing masks were applied to the time courses for each subject, removing on average approximately 6% of the time points from the pre-encoding scan, 9.5% from the post-encoding scan, and an average of 8% of time points across all five encoding scans.

To extract the background connectivity during the encoding scans, we low-pass filtered the encoding time series, removing signal at or above the task frequency (task frequency = 0.056 Hz, filter threshold = 0.045 Hz). The low-pass filter removed task-related fluctuations while keeping the low-frequency (background) signals that are more reflective of intrinsic activity (Newton, Morgan, Rogers, & Gore, 2011; Tambini, Rimmele, Phelps, & Davachi, 2016). Because low-pass filtering also removes high-frequency noise, leading to higher connectivity estimates (Van Dijk et al., 2010), we additionally low-pass filtered the rest timeseries at the same frequency when comparing connectivity across task and rest. Low-pass filtering was performed after computing FD and DVARS but before scrubbing of problematic timepoints.

Connectivity measures were obtained by partial correlations of the pre-processed, scrubbed timeseries between each of the memory ROIs and each of the five reward-related ROIs, controlling for WM, CSF, whole brain signal, motion parameters, and their derivatives. The resulting Pearson's r coefficients from the partial correlation analysis were Fisher z transformed to conform to the assumptions of normality before being submitted to further analyses. For the encoding scans, connectivity was measured and Fisher z transformed within each run. The normalized connectivity values were then averaged across the five encoding scans to produce a single measure of background connectivity during encoding.

Analysis of variance approach

To test whether connectivity patterns related to memory sensitivity to reward and whether this relationship is stable across task stages, the connectivity values were submitted to two repeated-measures ANOVAs. The first ANOVA only included rest data (pre-encoding, post-encoding), akin to prior work on resting state connectivity (Gruber et al., 2016). The second ANOVA included all three task stages (pre-encoding rest, encoding task, post-encoding rest), with low-pass filtered rest timeseries for comparison with task timeseries. In addition to task stage as a within-subject factor, both ANOVAs also included memory structure (hippocampus, PHC) and reward structure (ACC, midbrain, MPFC, OFC, VS) as within-subject factors and modulator status (modulator, nonmodulator) as a between-subjects factor.

The following effects were relevant to our questions of interest: (1) the main effect and interactions of modulator status, testing whether connectivity patterns relate to individual differences in memory sensitivity to reward; (2) the main effect and interactions of the task stage factor, testing the idea that connectivity patterns may be relatively stable across task and rest as well as track individual differences in memory sensitivity to reward; (3) the interactions of the reward region factor with the modulator status, testing whether all reward regions contribute similarly or differentially. Of note, the main effect of reward region and the main effect of memory region were not of interest as the overall functional connectivity value may depend on physical distance between regions and a

size of a region, and may not be easily interpretable (Honey et al., 2009; Salvador et al., 2005). When an interaction was found, we followed up with an investigation of the locus of the interaction. While the report focuses on the effects of interest, full ANOVA results are reported in tables. Greenhouse Geisser corrections were used when appropriate, reported in the tables as "GG." To validate that our findings were not driven by treating memory sensitivity to reward as a binary variable, we retested significant effects of interest from both ANOVAs using ANCOVA, with the continuous measure of behavioral reward modulation as a covariate.

Functional relationships among connections

Observing comparable or differential modulator effects across multiple reward ROIs in the ANOVAs provides one indication for unique or uniform contributions of reward regions to reward modulation of memory. To test more directly whether the reward regions are a part of the same functional network, we additionally examined their cross-correlational structure. We performed two principal component analyses: one on rest-only connectivity values (no low-pass filter to maintain information on high-frequency fluctuations), and one that included all of the connectivity values across task and rest (using low-pass filtered timeseries for comparable task and rest pre-processing). Components were considered for further analysis when they explained at least 10% of variance. For each considered component, we further tested the likelihood of obtaining such component by chance, using a comparison to a null distribution of components. To obtain the null distribution, we performed 10,000 simulated principal component analyses on data obtained by randomly shuffling connectivity values across participants, separately for each connection. The percent of variance explained by each component (first most informative, second most informative, etc.) was then compared to the null distribution's percent explained. The same results would be obtained by testing eigenvalues.

Loadings on each component were compared for the five reward ROIs using one-way ANOVA, and component scores were then related to behavioral reward modulation using multiple regression. Using dimensionality reduction before the multiple regression allowed us to test how underlying components, or potential networks of regions, contributed to the connectivity-behavior relationship while taking into account the collinearity between connectivity values and limiting in a data-driven manner the number of predictors considered.

Connectivity pattern classification

While traditional inference tests, such as analysis of variance, test the probability that observed differences between groups arose by chance alone, machine learning classification approaches allow us to quantify more directly how well the participants can be distinguished from one another based on their connectivity pattern. We used Support Vector Classification (SVC) to test the degree to which participants can be classified as either modulators or non-modulators based on their pattern of connectivity across the ten ROI connections (2 memory ROIs × 5 reward ROIs).

SVC was implemented using the "e1071" (Meyer, Dimitriadou, Hornik, Weingessel, & Leisch, 2017) statistical analysis package of R (https://www.r-project.org/) and conducted separately within each task stage. The default parameters for nu-classification were used (C = 1, ε = 0.1, γ = 0.1, no tuning) with a radial basis function kernel. We used a leave-one-subject-out cross-validation approach, training the model on N-1 subjects and then applying the trained classifier to predict the withheld subject's modulator status. The process was repeated as each subject in turn was withheld from the training set and used to test the model. The accuracy for the model was recorded as the percentage of correct classifications. A permutation test was used to test for significance. We conducted 5,000 simulations, each time randomly shuffling the modulator status labels across participants and then computing the same leave-one-subject-out cross-validated classification accuracy as with the real data. The true classifier accuracy was compared to the distribution of the simulated classification accuracies to derive the probability of obtaining such accuracy by chance alone. Accuracy that occurred with probability less than p = 0.017 was considered significant, reflecting Bonferroni correction across three task stages for an overall alpha = 0.05.

To verify the results were not driven by the median split approach, Support Vector Regression (SVR) was used to predict the continuous measures of behavioral reward modulation (BRM score) for each participant from connectivity measured at each task stage. The same statistical package, default parameters, and leave-one-subject out cross-validation approach were used for SVR as were used for SVC. The predicted BRM values for each subject were then correlated with the observed BRM values to assess whether the individual differences in connectivity patterns contain information about individual differences in behavioral reward modulation of memory. We employed Bonferroni corrections for the three correlations (alpha = 0.05/3 = 0.017).

Complementary connectivity analyses

In addition to the main questions of interests, the current study provides data suitable to address questions from prior studies on reward modulation of memory. We conducted two sets of exploratory analyses that maintain the focus on connectivity

and may be informative for the readers, even though they do not directly address the main goals of the study.

Correlations between connectivity changes and behavior The ANOVA, PCA, and machine learning approaches are well suited for testing the role of a broad set of reward regions and the connectivity fingerprint hypothesis, especially for the larger set of related connections considered here. In contrast, prior studies on reward modulation of memory have typically focused on single connections and learning-related effects, reporting first-order correlations relating pre-to-post encoding connectivity increases. While a disproportionate role of post-encoding rest could be indicated by a significant modulator by task stage interaction in our ANOVA, we also wanted to generate data directly comparable to prior studies. We thus additionally computed pre-to-post connectivity changes for each connection and correlated it with BRM. Because increased dopamine availability in the medial temporal lobe may enhance encoding in general (Duncan et al., 2014; Lisman et al., 2011), we also correlated the connectivity values with overall recall rates for each participant.

Anterior and posterior differences within hippocampus Previous work suggests there are functional differences between the anterior and posterior portions of the hippocampus (Brunec et al., 2018; McKenzie et al., 2014; Poppenk, Evensmoen, Moscovitch, & Nadel, 2013). In the context of reward motivated learning, however, evidence for differential contributions of anterior and posterior hippocampus is lacking or conflicting (Murty et al., 2017; Wolosin et al., 2013). We have performed exploratory analyses of anterior/posterior hippocampal connectivity patterns to test whether their connectivity patterns or connectivity changes are differentially related to behavior in our paradigm.

The middle slice of each participant's hippocampus ROI was used as a boundary for the anterior and posterior divisions. For participants that had an odd number of slices in their hippocampus ROI, the middle slice was assigned to the posterior portion. The ROIs were then used to extract the timeseries during each rest and task scan. Connectivity between anterior and posterior hippocampus with each reward region was measured using the procedures outlined above. Functional differences between anterior and posterior hippocampus were tested using repeated measures ANOVA with hippocampal ROI (anterior, posterior) × task stage (pre-encoding, encoding, post-encoding) × reward ROI (ACC, midbrain, MPFC, OFC, VS) as within-subject factors and modulator status as a between-subjects factor. Of main interest was the interaction between hippocampal ROI and modulator status, testing whether anterior and posterior hippocampus differentially related to reward modulation of memory.

Results

Behavioral results

Mean overall cued recall performance was 0.48 ($SD = 0.19$). A 2 (reward cue visual form) × 3 (reward cue value) repeated measures ANOVA revealed a marginally significant effect of reward value ($F(1.18, 27.03) = 3.86$, $p = 0.054$, $\eta^2_p = 0.14$, GG), with a significant quadratic ($F(1,23) = 9.93$, $p = 0.004$, $\eta^2_p = 0.30$) rather than a linear effect ($F(1,23) = 1.97$, $p = 0.174$). Follow-up pairwise comparisons revealed that the quadratic effect was driven by greater recall on dollar trials ($M = 0.53$, $SD = 0.20$; $t(23) = 2.41$, $p = 0.024$), and unexpectedly, penny trials ($M = 0.47$, $SD = 0.22$; $t(23) = 2.45$, $p = 0.022$) compared with dime trials ($M = 0.44$, $SD = 0.22$). The difference between dollar and penny trials did not reach significance ($t(23) = 1.40$, $p = 0.174$). There was no main effect of visual form ($F(1,23) = 0.04$, $p = 0.840$, $\eta^2_p = 0.002$) nor an interaction between form and value ($F(2,46) = 1.66$, $p = 0.202$, $\eta^2_p = 0.07$). Thus, accuracies were collapsed across visual form and used for all subsequent analyses. Cued recall rates for each reward value and form condition are presented in Fig. 3a.

A separate behavioral sample (n = 20) revealed a significant main effect of value ($F(1.23, 27.6) = 14.1$, $p = 0.001$, GG), comparably described as linear ($F(1,19) = 15.5$, $p = 0.001$) or quadratic ($F(1,19) = 10.8$, $p = 0.004$). Similar to the fMRI sample, cued recall accuracy was greater for dollar trials ($M = 0.61$, $SD = 0.19$) than for dime trials ($M = 0.44$, $SD = 0.21$; $t(19) = 3.83$, $p = 0.001$). Unlike the fMRI sample, the behavioral sample showed a memory advantage for dollar trials compared to penny trials ($M = 0.44$, $SD = 0.19$; $t(19) = 3.94$, $p = 0.001$) and no differences between penny and dime trials ($t(19) = 0.17$, $p = 0.87$).

While the U-shaped pattern of recall accuracies in the fMRI sample was unexpected and did not replicate in the separate behavioral sample, non-linear reward effects are plausible (Elliott, Newman, Longe, & Deakin, 2003). For example, penny trials may have been perceived as a loss relative to the (neutral) dime trials, making them more salient for encoding (Bartra, McGuire, & Kable, 2013; Seymour & McClure, 2008; Shigemune, Tsukiura, Kambara, & Kawashima, 2014; Tversky & Kahneman, 1981). Because the difference between dollar and penny trials was not significant and because both penny and dollar may have increased salience for individuals sensitive to reward, we instead used the memory advantage of dollar over dime trials (replicated across both behavioral and fMRI samples) as a measure of individual differences in memory sensitivity to reward. The raw dollar minus dime difference scores ranged from −0.25 to 0.75 (median of 0.07) and were not significantly correlated with the overall accuracy (Fig. 3b), suggesting that reward modulation of memory affected which events are
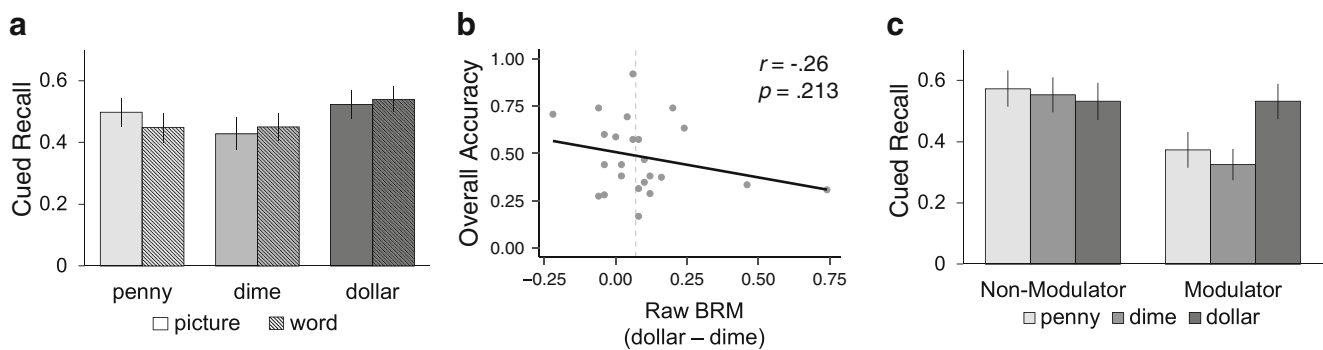
Fig. 3. Behavioral results. **a** Mean cued recall rates in each reward cue condition. **b** Correlation between overall accuracy and raw behavioral reward modulation (dollar minus dime) scores. **c** Mean cued recall rates for each reward value condition, separately for modulators and nonmodulators

preferentially remembered rather than providing an overall memory advantage. Because the raw difference scores were skewed by an outlier (>3 SD from the mean), we used a rank order of these scores in all subsequent analyses when correlating memory sensitivity to reward with connectivity measures. We refer to the dollar-dime difference score as *a raw behavioral reward modulation* (raw BRM) score and the rank-order measure used for all subsequent analyses as a *behavioral reward modulation* (BRM) score.

For visualization and analysis purposes, we also constructed a dichotomized measure of reward modulation of memory using a median split of BRM scores. This approach created two groups of participants that we refer to as modulators (sensitive to reward) and non-modulators (insensitive to reward). We performed confirmatory analyses to validate that the median split of participants yielded sensible groupings. Figure 3c shows cued recall accuracy per value, separately for each group. There was no effect of reward value in non-modulators (one-way ANOVA $F(1.15,12.7) = 1.36$, $p = 0.273$, GG), with raw BRM scores (dollar-dime difference) not different from zero ($M = -0.02$, $t(11) = -0.98$, $p = 0.348$), confirming that memory performance in this group was not significantly affected by reward value. In contrast, modulators showed an effect of reward value (one-way ANOVA $F(1.18,13.01) = 8.69$, $p = 0.009$, $\eta^2_p = 0.44$, GG), with greater accuracy for dollar trials than for dime trials (i.e., significant raw BRM scores; $M = 0.21$; $t(11) = 3.59$, $p = 0.004$), and greater accuracy for dollar trials than for penny trials ($t(11) = 2.43$, $p = 0.033$). Thus, the median split generated two sensible groups of participants that differ in their memory sensitivity to reward.

ANOVA results

Rest-only ANOVA We first addressed the relationship between rest connectivity and memory sensitivity to reward in a repeated-measures ANOVA with rest period (pre-encoding, post-encoding), memory ROI (hippocampus, PHC), and reward ROI (ACC, midbrain, MPFC, OFC, VS) as within-subjects factors and modulator status as a between-subjects

factor. The rest timeseries were not low-pass filtered for this analysis, as such a preprocessing step is not ordinarily applied during rest timeseries analyses as it may remove meaningful high-frequency fluctuations. All connections are depicted in Fig. 4a, and the complete ANOVA results are reported in Table 1.

Modulator status was marginally significant ($p = 0.051$), with modulators ($M = 0.36$, $SD = 0.10$), demonstrating numerically greater hippocampus/PHC-reward network connectivity than nonmodulators ($M = 0.29$, $SD = 0.06$). Modulator status significantly interacted with reward structure. This interaction was driven by greater hippocampus/PHC connectivity with ACC, OFC, and VS in modulators than nonmodulators (all $t > 2.15$, all $p < 0.045$), with no effect of modulator status in hippocampus/PHC-midbrain and hippocampus/PHC-MPFC connectivity (both $t < 1.4$, $p > 0.18$). When reward modulation of memory was treated as a continuous measure using ANCOVA, the results were similar but weaker. The main effect of BRM ($r(22) = 0.35$; $F(1,22) = 3.12$, $p = 0.091$, $\eta^2_p = 0.12$) remained marginally significant, but the interaction between reward structure and BRM did not ($F(2.83,62.22) = 1.99$, $p = 0.128$, GG).

The ANOVA additionally revealed a main effect of rest period, with connectivity increasing from the pre-encoding ($M = 0.30$, $SD = 0.10$) to post-encoding rest scan ($M = 0.36$, $SD = 0.11$). Rest period did not interact with modulator status ($p > 0.6$) or BRM in the ANCOVA ($p > 0.3$), indicating that although the overall connectivity increased from pre-encoding to post-encoding, its relationship to behavior did not change significantly.

Omnibus ANOVA across rest and encoding task To compare rest connectivity with background task connectivity, we used connectivity measures from low-passed filtered timeseries to match task and rest preprocessing. Connectivity measures were submitting to the same ANOVA as reported above, with the task stage factor having three values (pre-encoding, encoding, post-encoding). This analysis allows us to directly test the hypothesis that patterns of connectivity and their relationship to behavior are stable across task and rest. The results
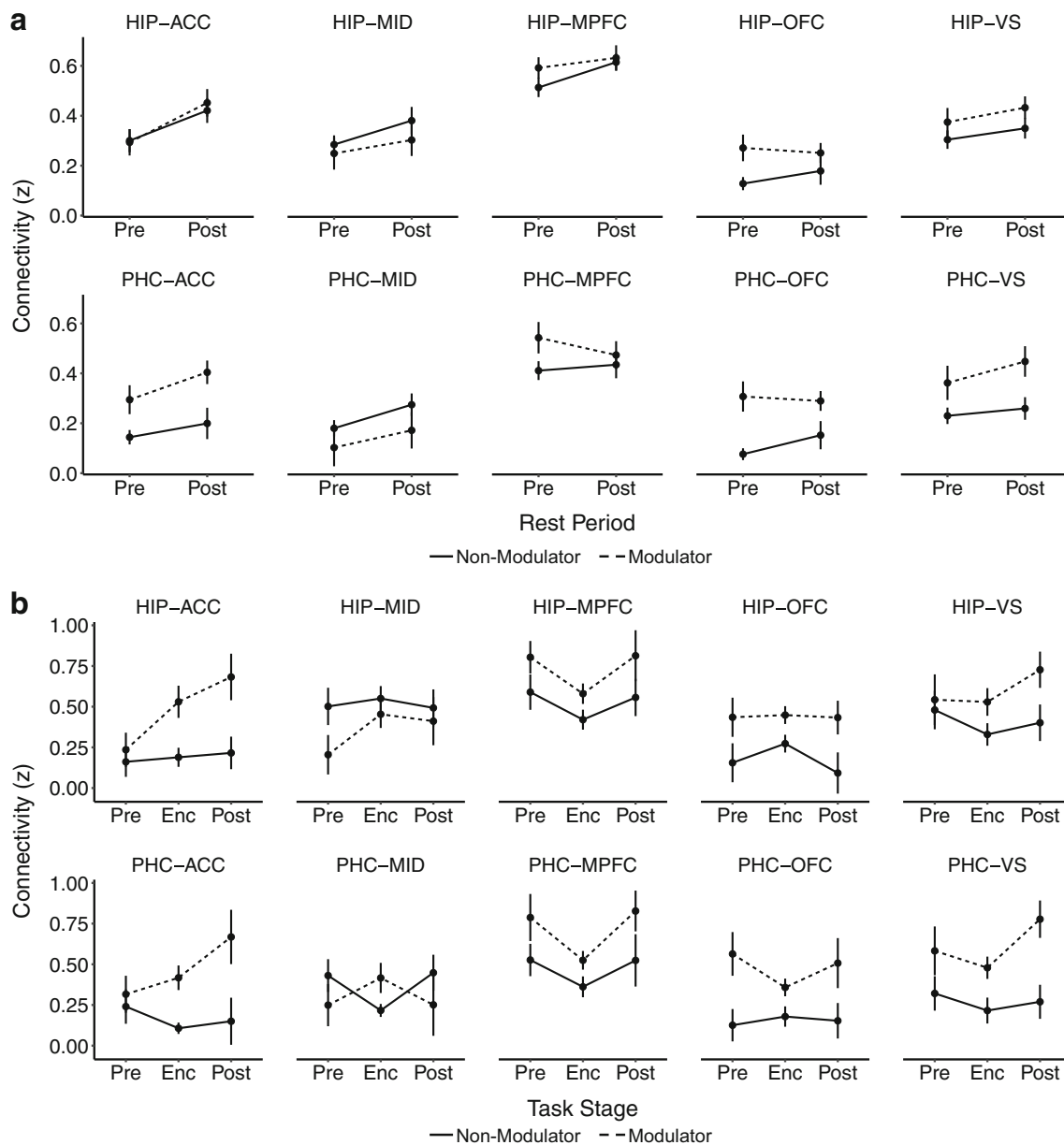
Fig. 4. ANOVA results. **a** Pre-encoding and post-encoding connectivity between memory (hippocampus, PHC) and reward (ACC, midbrain, OFC, VS, MPFC) ROIs are shown separately for modulators and non-modulators. **b** Low-frequency background connectivity between memory and reward ROIs are plotted across the three task stages (pre-encoding, encoding, post-encoding) separately for modulators and non-modulators. HIP = hippocampus; MID = midbrain

of the ANOVA are reported in Table 2, and all connectivity values are depicted in Fig. 4b. From the effects of interest, we found a main effect of modulator status, with greater connectivity in modulators ($M = 0.52$, $SD = 0.14$) than non-modulators ($M = 0.32$, $SD = 0.21$). We also found a significant interaction between modulator status and reward structure. Follow-up two-sample t-tests showed that the interaction was driven by significant differences between modulators and non-modulators in hippocampus/PHC connectivity with ACC, MPFC, OFC, and VS (all $t(22) > 2.1$, $p < 0.05$) but not with midbrain ($t(22) = 0.90$, $p = 0.377$). The effect of modulator status and the

interaction between modulator status and reward structure were not driven by a median split of participants and were replicated when memory sensitivity to reward was treated as a continuous measure using ANCOVA (main effect of BRM: $F(1,22) = 7.13$, $p = 0.014$, $\eta^2_P = .25$; BRM*reward structure interaction: $F(2.80,61.58) = 3.25$, $p = 0.031$). We found no effect of task stage and no interaction between task stage and modulator status in this analysis (both $p > 0.2$), suggesting connectivity between memory and reward networks and its relationship to behavior remained relatively stable across the pre-encoding, encoding, and post-encoding scans.

Table 1 Rest-only ANOVA

Source	df_{effect}	df_{error}	F	p	η_p^2
Modulator	1	22	4.26	0.051	0.16
Task stage*	1	22	6.33	0.020	0.22
Task stage × modulator	1	22	0.24	0.630	0.01
Memory ROI***	1	22	18.16	0.000	0.45
Memory ROI × modulator	1	22	3.21	0.087	0.13
Reward ROI *** (GG)	3.03	66.72	31.93	0.000	0.59
Reward ROI × modulator* (GG)	3.03	66.72	3.78	0.014	0.15
Task stage × memory ROI	1	22	0.95	0.340	0.04
Task stage × memory ROI × modulator	1	22	0.01	0.932	0.00
Task stage × reward ROI	4	88	1.78	0.140	0.08
Task stage × reward ROI × modulator	4	88	1.15	0.339	0.05
Memory ROI × reward ROI** (GG)	2.84	62.46	4.36	0.008	0.17
Memory ROI × reward ROI × modulator (GG)	2.84	62.46	1.91	0.141	0.08
Task stage × memory ROI × reward ROI (GG)	2.50	55.05	2.17	0.112	0.09
Task × Memory × Reward × Modulator (GG)	2.50	55.05	0.23	0.842	0.01

The rest ANOVA examined memory structure (HIP, PHC), reward structure (ACC, MID, OFC, VS, MPFC), rest period (pre-encoding, post-encoding) and modulator status (modulator, nonmodulator). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Summary of the ANOVA findings Both omnibus and rest-only ANOVAs showed an effect of modulator status on memory-reward region connectivity and revealed that the modulator effect was not driven by all connections equally. A set of reward regions disproportionately drove the overall effect: ACC, OFC, and VS connectivity with hippocampus/PHC consistently differed between modulators and nonmodulators, whereas midbrain connections consistently did not. While we found an overall increase in connectivity between reward and memory regions from pre-encoding to post-encoding in the rest-only ANOVA, there were no interactions between modulator status and task stage in either analysis. These results are consistent with the idea that there are stable individual differences in brain connectivity patterns that relate to behavior.

Table 2 Omnibus ANOVA

Source	df_{effect}	df_{error}	F	p	η_p^2
Modulator*	1	22	7.15	0.014	0.25
Task stage	2	44	1.44	0.248	0.06
Task stage × modulator	2	44	1.10	0.343	0.05
Memory ROI	1	22	3.75	0.066	0.15
Memory ROI × modulator	1	22	2.59	0.122	0.11
Reward ROI *** (GG)	2.87	63.24	9.69	0.000	0.31
Reward ROI × modulator** (GG)	2.87	63.24	4.78	0.005	0.18
Task stage × memory ROI (GG)	1.53	33.67	2.00	0.159	0.08
Task stage × memory ROI × modulator (GG)	1.53	33.67	0.19	0.765	0.01
Task stage × reward ROI	8	176	1.92	0.060	0.08
Task stage × reward ROI × modulator	8	176	1.53	0.150	0.07
Memory ROI × reward ROI	4	88	1.35	0.256	0.06
Memory ROI × reward ROI × modulator	4	88	0.61	0.656	0.03
Task stage × memory ROI × reward ROI (GG)	4.84	106.4	0.69	0.631	0.03
Task × memory × reward × modulator (GG)	4.84	106.4	0.97	0.436	0.04

The omnibus ANOVA examined the effects of memory structure (HIP, PHC), reward structure (ACC, MID, MPFC, OFC, VS), task stage (pre-encoding, encoding, post-encoding), and modulator status (nonmodulator, modulator). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$
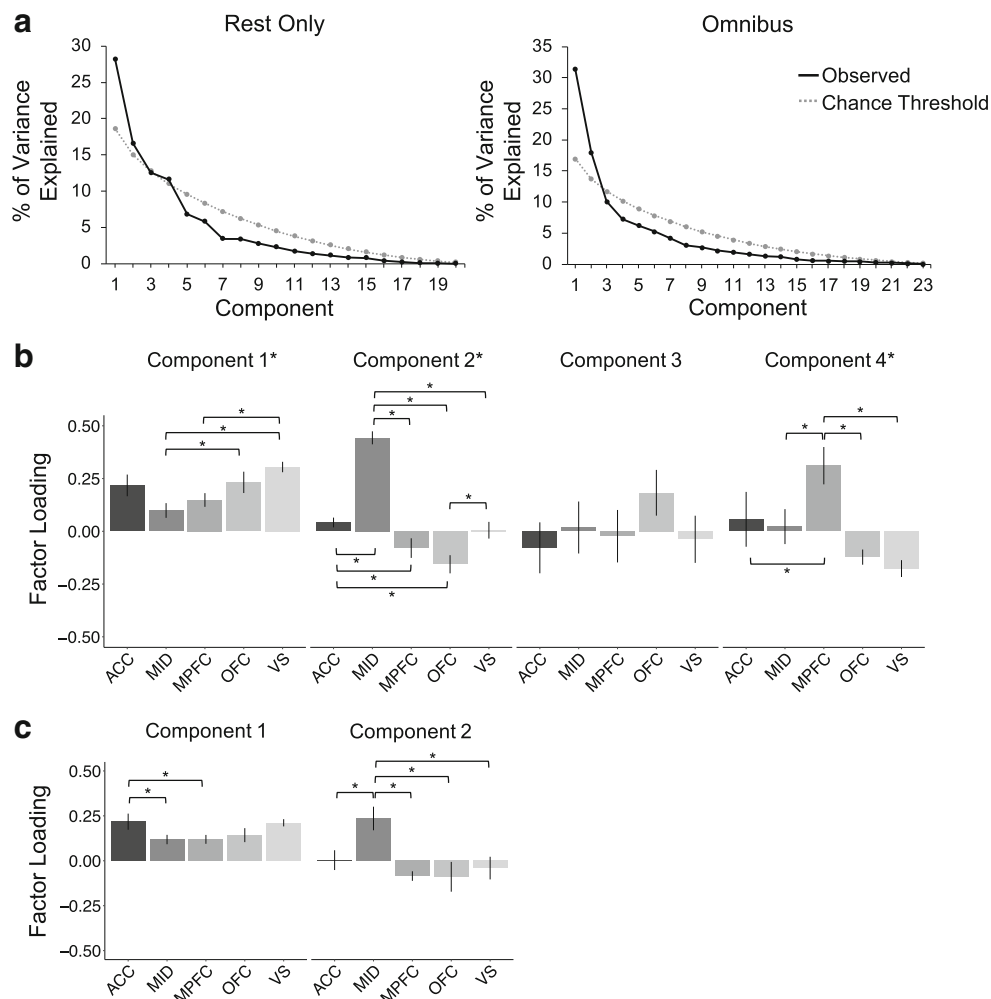
Functional relationships among connections

Rest-only PCA To investigate which reward regions may be a part of the same functional network, we investigated the cross-correlation structure of connectivity values across participants. Pairwise correlations of all rest-based connectivity values are presented in Fig. 5a. After separating them into principal components, we found four components that explained at least 10% of variance in the connectivity values and were retained for further analyses (Fig. 5b). Monte Carlo simulations (Fig. 6a) indicated that all components explained more variance than expected by chance (all $p < 0.01$), except for component 3, which was marginal ($p = 0.083$). Preferential loading of

each reward region on different components was tested using one-way ANOVA (Fig. 6b).

The first component explained 28.2% of variance in connectivity scores and loaded preferentially on ACC, OFC, and VS connections and, to a lesser extent, MPFC and midbrain (one-way ANOVA, $F(4,15) = 3.91$, $p = 0.023$). The second component explained 16.6% of variance and was loading preferentially on midbrain connections and, to a lesser extent, negatively on OFC and MPFC connections (one-way ANOVA, $F(4,15) = 38.2$, $p < 0.001$). The third component explained 12.5% of variance and loaded comparably across all reward regions (one-way ANOVA $F(4,15) = 0.74$, $p = 0.580$). The fourth component explained 11.6% of variance and was

Fig. 5. Relationships among connections. **a** Pairwise, cross-participant correlations of all rest-based connectivity measures. **b** Loadings of each pre-encoding and post-encoding connection on the four components that were generated by PCA

Fig. 6. The loadings of each reward ROI's connections on PCA generated components. **a** The percent of variance explained by each component in both the rest only PCA (left) and omnibus PCA (right). The gray dotted line denotes the upper threshold for chance ($p < 0.05$) of percent explained by each component. **b** The relative contribution of each reward ROI (ACC, MID, MPFC, OFC, VS) on each of the four retained PCA-derived components on pre-encoding and post-encoding resting state connectivity between memory and reward ROIs. **c** The relative contribution of each reward ROI on the two retained components derived from the omnibus PCA across task and rest. In both **b** and **c**, bars with stars denote significant pair-wise differences in loadings

loading preferentially on MPFC connections (one-way ANOVA $F(4,15) = 5.26$, $p = 0.008$). Multiple regression then tested the relationship between the component scores and behavioral reward modulation across participants. The first component score significantly tracked behavioral reward modulation (beta = 7.09, $SE = 3.13$, $p = 0.03$) while the remaining components did not (all $p > 0.18$). These results indicate ACC, OFC and VS connectivity with hippocampus/PHC co-vary and jointly track memory sensitivity to reward. Midbrain and MPFC connectivity covaried to a lesser degree with the other reward-related regions and with each other. Furthermore, the components that midbrain and MPFC most strongly loaded on did not track memory sensitivity to reward, opening the possibility that they may each be a part of functionally different systems.

The lack of differentiation between modulators and nonmodulators based on hippocampus/PHC-midbrain was

unexpected, especially given that significant effects of connectivity were observed for other reward-related regions in both ANOVA and PCA. While reward modulatory effects on midbrain interactions with memory regions have been documented previously (Gruber et al., 2016; Wolosin et al., 2012), the effect may not result in increased sensitivity to reward per se. Instead, overall greater interactions—irrespective of external rewards—may lead to greater dopamine availability in the hippocampus and greater memory overall (Duncan et al., 2014; Lisman et al., 2011; Tompary et al., 2015).

To test this idea, we performed a second multiple regression with component scores as predictors but this time using overall accuracy as an outcome. The second component significantly predicted the overall accuracy across participants (beta = 0.28, $SE = 0.11$, $p = 0.02$), while the other three components did not (all $p > 0.5$). Thus, a distinct pattern of resting state connectivity, captured by the second component loading

preferentially on the hippocampus/PHC-midbrain connectivity, also was relevant to behavior but tracked overall memory rather than memory sensitivity to reward.

Omnibus PCA across task and rest To test the degree to which cross-correlations may remain stable across task and rest, a second PCA was performed on the whole set of 30 connectivity values per subject (10 connections for each pre-encoding, encoding, and post-encoding periods). Connectivity values derived from low-pass filtered timeseries were used to match pre-processing across task and rest. Three components explained more than 10% of variance. Monte Carlo simulations (Fig. 6a) indicated that only components 1 and 2 explained more variance than expected by chance (both $p < 0.001$). Component 3 did not ($p = 0.8$) and thus was not considered further. The loadings of each reward regions on the two retained components are presented in Fig. 6c.

The first component explained 31.4% of variance and showed marginal differences between loadings among reward regions (one-way ANOVA $F(4,25) = 2.30$, $p = 0.086$), with numerically greatest loadings of ACC and VS. The second component explained 18.0% of variance and most strongly loaded on midbrain connections ($F(4,25) = 4.78$, $p = 0.005$). Multiple regression with component scores as predictors and BRM as an outcome showed that the first component was a significant predictor of BRM (beta = 2.99, $SE = 1.00$, $p = 0.007$), while the other was not ($p > 0.09$). A second multiple regression with the overall accuracy as an outcome did not reveal any significant effects (all $p > 0.2$). Thus, the omnibus PCA partially replicated the rest-only PCA. Taken together, the PCA findings indicate that: (1) connectivity patterns of ACC, VS, and potentially OFC are functionally coupled, with a composite connectivity score that most strongly loaded on these regions tracking memory sensitivity to reward, (2) midbrain and potentially MPFC connectivity patterns co-vary to a lesser degree with the other reward regions and each other, and (3) resting state hippocampus/PHC-midbrain connectivity may be more predictive of overall memory performance than memory sensitivity to reward.

Predicting memory sensitivity to reward from connectivity patterns using machine learning

The ANOVA and PCA findings reported above showed that connectivity between memory and reward-related regions tracked individuals' memory sensitivity to reward and that this relationship may be relatively preserved irrespective of task stage. To more directly quantify how well patterns of connectivity may differentiate between modulators and nonmodulators, we applied SVC to predict modulator status from connectivity patterns in each task stage (inputs = 10 connectivity values, outputs = modulator status). Classification accuracy that occurred with a probability of less than 0.017 (0.05/

3 to correct for multiple comparisons) was considered significant. Using cross-validation, we found that classification of modulator status from connectivity patterns was reliably above chance in the pre-encoding scan (accuracy = 79.2%, $p = 0.010$) and the encoding scan (accuracy = 75%, $p = 0.006$). Classification based on the post-encoding scan was lower and not reliably different from chance (accuracy = 58.3%, $p = 0.157$; Fig. 7a). Although the classification accuracy based on post-encoding connectivity did not reach significance, we did not find evidence that the probability of misclassification would be reliably greater at post-encoding compared to pre-encoding or encoding task stages (both $\chi^2 < 2.1$, $p > 1.5$).

To verify that successful classification did not depend on treating reward modulation as a dichotomized variable, ε-SVR was conducted to predict behavioral reward modulation as a continuous measure. Consistent with the SVC findings, cross-validated SVR revealed that connectivity between memory and reward regions reliably predicted BRM during the encoding scan ($r = 0.51$, $p = 0.010$), and marginally predicted during the pre-encoding rest scan ($r = 0.46$, $p = 0.024$). The SVR on post-encoding connectivity did not reach significance ($r = 0.35$, $p = 0.098$; Fig. 7b).

Complementary connectivity analyses

Correlations between connectivity changes and behavior Though we did not find interactions between task stage and reward modulation of memory in the rest-only ANOVA, a changing relationship between connectivity and behavior may be better characterized by a correlation of task-induced increases in connectivity with behavior (Gruber et al., 2016; Murty et al., 2017; Tambini et al., 2010). To test the effect of connectivity increases on behavior, we ran exploratory correlations between pre-to-post connectivity increases and both BRM and overall accuracy (Table 3). None of the memory-reward ROI connections predicted BRM (all $p > 0.15$, uncorrected for multiple comparisons) nor overall cued recall rates (all uncorrected $p > 0.05$). There was a marginal correlation between PHC-midbrain connectivity and overall accuracy (r = 0.40, $p = 0.052$), providing a partial replication of prior reports on midbrain connectivity changes tracking behavior (Duncan et al., 2014; Gruber et al., 2016).

Anterior and posterior differences within hippocampus Functional differences between anterior and posterior hippocampus were tested in a 3 (task stage) × 2 (hippocampus ROI: anterior, posterior) × 5 (reward ROI) repeated measures ANOVA with modulator status as a between-subjects factor. The results for the ANOVA are reported in Table 4, and all connections are displayed in Fig. 8. We found a main effect of modulator status, indicating that hippocampal connectivity with reward regions tracked memory sensitivity to reward. We also found a significant interaction between reward ROI
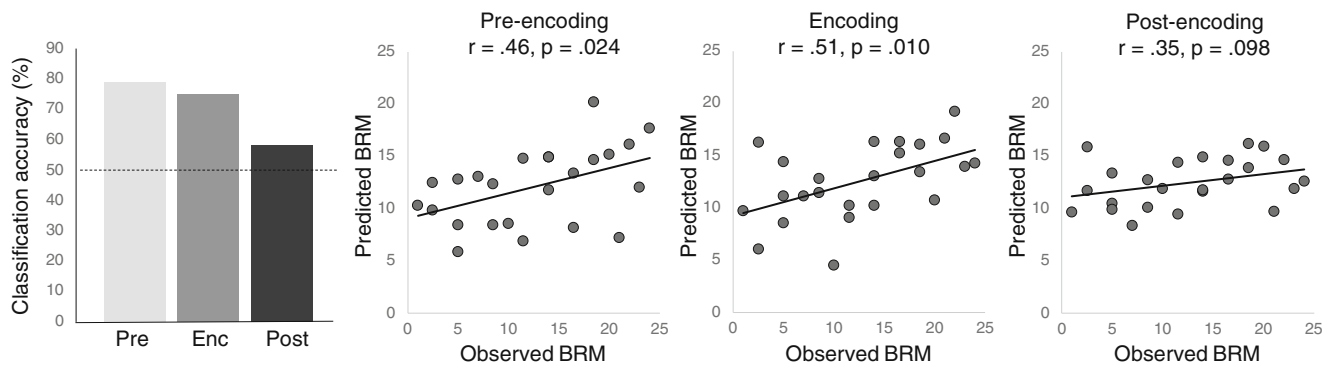
Fig. 7. Predicting memory sensitivity to reward from connectivity patterns. **a** Support vector classification accuracy of connectivity predicting modulator status at each of the task stages. The classifier accuracy for both pre-encoding and encoding connectivity were reliably above chance (indicated by the dashed line), as determined by a permutation test. **b** Comparison of observed BRM and predicted BRM by support vector regression at each task stage

and hippocampal division, indicating that anterior and posterior hippocampus are preferentially connected to distinct reward regions. Of main interest were interactions between hippocampal division and modulator status that would indicate that anterior and posterior portions of the hippocampus differentially predict reward modulation of memory. However, all interactions that included modulator status and hippocampal ROI as factors were non-significant (all $F < 1.5$, $p > 0.3$), providing no evidence for such dissociation.

As a last analysis, we tested whether connectivity increases from pre- to post-encoding rest may be differentially related to behavior for anterior and posterior hippocampus. Thus, we correlated BRM with post-pre connectivity changes in each connection, separately for anterior and posterior hippocampus. No significant correlations were found (all $|r| < 0.32$, all $p > 0.05$).

Discussion

The current study measured functional connectivity between memory and reward regions before, during, and after a monetary incentive encoding task. Using both standard and

Table 3 Correlations of post–pre resting connectivity changes with behavior

Connection	BRM (r)	Accuracy (r)
HIP-ACC	0.07	0.15
HIP-MID	-0.05	0.13
HIP-MPFC	-0.24	0.24
HIP-OFC	-0.16	0.11
HIP-VS	-0.26	-0.28
PHC-ACC	0.08	0.07
PHC-MID	-0.14	0.40
PHC-MPFC	-0.34	0.02
PHC-OFC	-0.23	0.30
PHC-VS	-0.13	0.12

machine learning approaches, we observed that connectivity of hippocampus and PHC with reward-related regions tracked individual differences in memory sensitivity to reward. This effect was differentially driven by a subset of reward regions: ACC, OFC, and VS connectivity patterns co-varied together across participants and were consistently predictive of individual differences in reward modulation of memory. Midbrain connectivity with hippocampus and PHC was not related to memory sensitivity to reward, and the MPFC connectivity with memory regions varied across analyses. The relationship between connectivity and reward modulation of memory was present prior to encoding and during encoding, with weaker but not reliably different effects during post-encoding rest. Overall connectivity between memory and reward regions increased from pre- to post-encoding rest, but connectivity changes were not significantly related to behavior. These results demonstrate stable individual differences in intrinsic communication between memory and reward-related regions that track individual differences in reward modulation of memory. Furthermore, the results implicate a wider set of reward-related regions in memory modulation by reward than previously considered.

Theoretical perspectives have emphasized the role of midbrain, and to some degree VS, in memory modulation by reward (Lisman & Grace, 2005). A central finding of the current study is that connectivity of reward regions VS, ACC, and OFC with hippocampus and PHC was related to the degree to which individuals' memory was impacted by reward. The role of VS in reward modulation of memory is predicted by current models, which postulate that VS integrates and relays dopamine signals from the hippocampus to the midbrain (Lisman & Grace, 2005). A prior study on reward-motivated encoding found univariate activation in VS covaried with hippocampus and PHC, further tracking the impact of reward on memory (Adcock et al., 2006). Our study, however, is the first to show connectivity between VS, jointly with OFC and ACC, and memory centers in hippocampus and PHC predicted individual differences in reward modulation of memory, irrespective

Table 4 Anterior versus posterior hippocampus ANOVA table

Source	df_{effect}	df_{error}	F	p	η_p^2
Modulator*	1	22	4.96	0.037	0.18
Task stage	2	44	0.86	0.431	0.04
Task stage × modulator	2	44	1.49	0.237	0.06
Hippocampus ROI	1	22	1.89	0.183	0.08
Hippocampus ROI × modulator	1	22	0.03	0.856	0.00
Reward ROI***	4	88	6.07	0.000	0.22
Reward ROI × modulator*	4	88	3.56	0.010	0.14
Task stage × hippocampus ROI	2	44	0.12	0.892	0.01
Task stage × hippocampus ROI × modulator	2	44	1.23	0.302	0.05
Task stage × reward ROI	8	176	1.93	0.058	0.08
Task stage × reward ROI × modulator	8	176	0.65	0.738	0.03
Hippocampus ROI × reward ROI (GG)***	2.91	63.97	10.53	0.000	0.32
Hippocampus × reward ROI × modulator (GG)	2.91	63.97	0.61	0.609	0.03
Task stage × hippocampus × reward ROI (GG)**	4.04	88.93	4.04	0.005	0.16
Task × hippocampus × reward × modulator (GG)	4.04	88.93	1.06	0.382	0.05

ANOVA included within-subject effects of task stage (pre-encoding, encoding, post-encoding), hippocampus ROI (anterior, posterior), and reward ROI (ACC, midbrain, MPFC, OFC, VS), with modulator status (nonmodulator, modulator) as a between-subjects factor. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

of when connectivity was measured. Interestingly, background VS-hippocampal connectivity is also observed in procedural learning when procedural learning is rewarded (Hamann, Dayan, Hummel, & Cohen, 2014). Thus, while the traditional multiple memory systems view postulates a division of labor between hippocampus, supporting declarative memory, and striatum, supporting procedural memory (Squire, 1992), there may be a strong degree of interactions between these systems supporting both episodic memory and procedural learning (Doll, Shohamy, & Daw, 2015; Hamann

et al., 2014; Kafkas & Montaldi, 2015; Wimmer, Daw, & Shohamy, 2012).

Our study also implicated two reward regions previously not considered in the context of reward motivated learning—the OFC and ACC—which showed similar profiles to VS. While novel in the area of reward modulation of memory, prior work has reported hippocampal connectivity with ventromedial/orbitofrontal regions across various contexts of learning (Gluth, Sommer, Rieskamp, & Büchel, 2015; Ranganath, Heller, Cohen, Brozinsky, & Rissman, 2005;
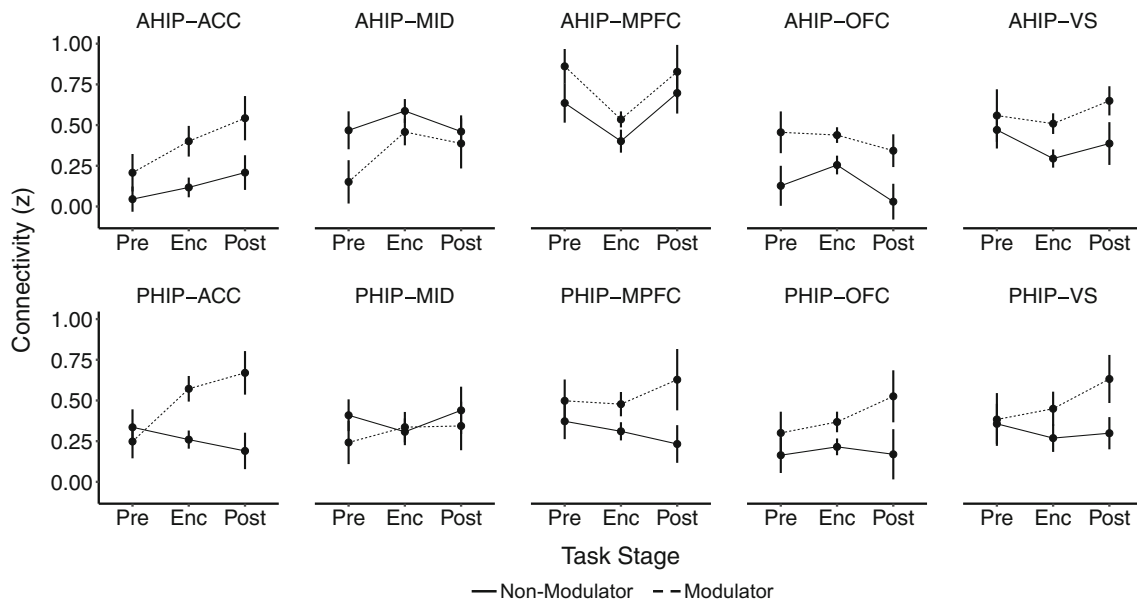

Fig. 8. Connectivity of anterior and posterior hippocampus with reward ROIs. Background connectivity between reward ROIs and anterior/posterior hippocampus across the three task stages are presented separately for modulators and non-modulators

Tsukiura & Cabeza, 2008; Zeithamova, Dominick, & Preston, 2012). For instance, background hippocampal-OFC connectivity inversely tracks transfer of learned reward to related experiences (Gerraty et al., 2014). In a sensory preconditioning paradigm, participants encoded face-face pairs and then were trained to associate a gain, loss, or no value with one of the faces. Hippocampal-OFC connectivity was negatively correlated with transfer, meaning that participants with stronger connectivity showed lesser tendency to extend the learned face value to related faces. Thus, although the role of interactions between memory regions and OFC may vary depending on the specific task, our study converges with prior work to show that participants with greater hippocampal-OFC connectivity are more likely to differentiate events based on their explicitly assigned values.

The functional relevance of ACC in memory in humans is currently less understood. During rest, ACC demonstrates functional connectivity with both hippocampus and PHC (Cao et al., 2014; Margulies et al., 2007). In rodents, the ACC has been implicated in consolidation of learned associations into long-term memory, showing coordinated cellular changes with the hippocampus (Wang, Tse, & Morris, 2012; Weible, Rowland, Monaghan, Wolfgang, & Kentros, 2012). Here, ACC, OFC, and VS connectivity with hippocampus and PHC covaried across participants. While intrinsic, coordinated activity between the hippocampus, ventral striatum, and OFC has been reported previously (Gerraty et al., 2014; Kahn & Shohamy, 2013), our data implicate that ACC may comprise a functional network with VS and OFC.

Although ACC and OFC may show distinct functions in some tasks (Luk & Wallis, 2013), the ACC, OFC, and VS all share similar functions during reward processing, such as tracking anticipated reward values and outcomes (Amiez et al., 2006; Bialleck et al., 2011; Knutson, Taylor, Kaufman, Peterson, & Glover, 2005; Yan et al., 2016) and signaling the value of choices (Boorman, Behrens, Woolrich, & Rushworth, 2009; Rogers et al., 2004; Strait, Blanchard, & Hayden, 2014). Together, these regions may serve to promote motivationally salient behaviors or suppress motivationally irrelevant behaviors (Hare, O'Doherty, Camerer, Schultz, & Rangel, 2008; Kaping, Vinck, Hutchison, Everling, & Womelsdorf, 2011; Nieuwenhuis & Takashima, 2011; O'Doherty, 2011; Walton, Chau, & Kennerley, 2015). Greater background hippocampal and PHC interactions with ACC, OFC, and VS may reflect greater availability of reward signals to memory structures, resulting in enhanced modulation of memory by reward in our paradigm. While the unique contribution of each region will require further inquiries into their individual roles in motivated learning, our data provide several new insights into their functional interactions.

An unexpected aspect of the current data was the U-shaped relationship between reward value and memory found in the fMRI sample. While this finding was unexpected and not replicated in the accompanying behavioral sample, it is neurobiologically plausible. U-shaped responses to reward have been identified in the medial frontal and medial orbitofrontal cortices (Elliott et al., 2003): notably, regions, such as the ACC and VS, signal the reward prediction error, or the discrepancy between expected and experienced rewards (Abler, Walter, Erk, Kammerer, & Spitzer, 2006; Fiorillo, Tobler, & Schultz, 2003; Montague, Dayan, & Sejnowski, 1996; Silvetti, Seurinck, & Verguts, 2011). These signals do not reflect the absolute value of losses and gains but rather the relative value, flexibly scaling around an expected reference point (Seymour & McClure, 2008; Tobler, Fiorillo, & Schultz, 2005). In the current task, the dime trials may have served as a reference condition, with dollar trials being perceived as rewards and penny trials as relative losses. The salience of both losses and gains can impact performance (Bartra et al., 2013; Shigemune et al., 2014), manifesting as the U-shape in cued recall accuracy across the reward conditions. Taken together, reward effects on memory may reflect the influence of reward prediction error signals on encoding, which may be non-linear in nature.

Contrary to prior studies, we did not find a relationship between hippocampal-midbrain connectivity and reward modulation of memory, even when the hippocampus was separated into anterior and posterior sections (Adcock et al., 2006; Gruber et al., 2016; Murty et al., 2017; Wolosin et al., 2012). Rather, we found a correlation between a component score from the PCA that loaded preferentially on midbrain-hippocampus/PHC connections and overall accuracy. While this finding was not expected *a priori*, it is consistent with the proposal that interactions between midbrain and medial temporal regions are not unique to externally motivated rewards but support encoding and consolidation in general (Lisman et al., 2011). Consistent with this view, midbrain has been shown to interact with hippocampus in encoding tasks that do not involve reward (Duncan et al., 2014; Zeithamova, Manthuruthil, & Preston, 2016), with both background connectivity during encoding (Duncan et al., 2014) and rest connectivity after encoding (Tompary et al., 2015) tracking associative memory. Our findings suggest that midbrain connectivity during reward motivated encoding may be more relevant to overall associative memory than reward modulation of memory and potentially plays a distinct functional role in memory from other reward-related regions.

Of note is the relatively short delay between encoding and test in our paradigm that also may affect the pattern of midbrain effects observed. Reward-related memory effects have been documented during immediate tests of memory (Gruber et al., 2016; Wolosin et al., 2012, 2013) but appear stronger after overnight consolidation (Patil, Murty, Dunsmoor, Phelps, & Davachi, 2017; Tompary et al., 2015; Wittmann et al., 2005). The delayed impact of reward on memory performance is thought to reflect enhancement of dopamine-

dependent consolidation processes by rewards (Lisman et al., 2011). Thus, while midbrain interactions with hippocampus and PHC predicted overall memory in our paradigm, it is possible that an additional midbrain contribution to reward-enhanced consolidation would be observed if recall had been performed after a 24-hour interval had elapsed.

One reward region that did not show a consistent relationship to behavior in our paradigm was MPFC. Connectivity with MPFC was predictive of memory sensitivity to reward in the omnibus ANOVA across rest and task, but the relationship to behavior did not replicate in other analyses. Although prefrontal reward regions like OFC and MPFC are spatially proximal and often considered together, the PCA results indicate that they may participate in partially distinct networks. A more conclusive characterization of the role of MPFC in motivated encoding and memory in general awaits future studies.

In addition to implicating a broader set of reward regions in motivated encoding than previously considered, a second key contribution of our study is novel evidence for the connectivity fingerprint hypothesis (Finn et al., 2015; Gratton et al., 2018). Measuring patterns of connectivity before, during, and after motivated encoding, we found that individual differences in reward modulation of memory were predicted by connectivity between memory and reward regions, irrespective of when connectivity was measured. Though post-encoding connectivity was less consistently related to behavior, we found no reliable differences in predictability of behavior between the task stages. These results are in line with the recent findings of stable connectivity patterns and their relationship to individual differences in cognition (Finn et al., 2015; Gratton et al., 2018; Poole et al., 2016; Touroutoglou, Andreano, Barrett, & Dickerson, 2015; Wang et al., 2010), newly extending them to the area of motivated encoding.

Our focus on stable, individual differences in connectivity complement other approaches to linking connectivity to behavior, including memory. Resting state functional connectivity can change on a short time-scale in response to a task (Tambini et al., 2010; Urner, Schwarzkopf, Friston, & Rees, 2013), with learning-related connectivity changes relating to memory performance (Gruber et al., 2016; Murty et al., 2017; Tambini et al., 2010; Urner et al., 2013). During task performance, across-region coupling may change even more rapidly, differentiating between memory task conditions at the order of minutes or even from individual trial to individual trial (Kafkas & Montaldi, 2015; Rissman, Gazzaley, & D'Esposito, 2004; Zeithamova et al., 2012; Zeithamova et al., 2016). For example, Kafkas and Montaldi (2015) showed that hippocampal-VS connectivity was greater during encoding of unexpected versus expected stimuli. Thus, both the stable and variable aspects of connectivity provide information relevant to cognition.

Which aspects of connectivity (stable or task-induced) are more pronounced or most relevant to behavior is an open question (Gratton et al., 2018) but may depend on the task and the specific region. For example, Gruber et al. (2016) found reward modulation of memory related to task-induced connectivity changes, whereas we found that stable connectivity patterns predicted behavior. Regarding task differences, the Gruber et al. (2016) study tested incidentally encoded scene-object associations, with four possible scenes repeated many times across encoding. Two scenes were always low-value and two high-value. Performance on a forced-choice test asking which of the four scenes was previously associated with a given object (with "unsure or new" as a fifth option) could thus partially rely on remembering the object's value, which is plausible given that object-scene memory was relatively close to chance. In contrast, the present study required intentional encoding of trial-unique object pairs, with trial value being unrelated to the memoranda. Regarding regional differences, Gruber et al. (2016) found midbrain connectivity changes that tracked behavior, which was partially replicated in our data. In contrast, we found stable connectivity patterns of other reward-related regions with memory regions to relate to behavior. Although speculative at this time, these commonalities and differences across findings open up a new avenue for inquiry regarding the factors that determine how stable vs. dynamic aspects of connectivity may relate to different aspects of cognition.

Complementary to our main questions of interest, we further conducted an exploratory analysis of potential functional differences between the anterior and posterior hippocampus. While anterior/posterior differences have been previously documented in various memory paradigms (Bowman & Zeithamova, 2018; Brunec et al., 2018; McKenzie et al., 2014; Poppenk et al., 2013), the evidence within the domain of motivated encoding is sparse and varying. For example, Murty et al. (2017) reported a stronger link between anterior hippocampal connectivity and behavior while Wolosin et al. (2013) found reward modulation effect in posterior hippocampus. We found anterior/posterior differences with respect to connectivity with distinct reward regions, however, the relationship to memory sensitivity to reward was comparable for anterior and posterior hippocampus. These studies indicate that reward modulation of memory may not be strongly dissociated along the anterior/posterior axis.

In summary, the current study significantly expands our understanding of motivational influences on memory, newly demonstrating the role of stable, individual differences in connectivity in predicting how individual's memory is impacted by reward. The results also demonstrate a role for several reward-related regions in motivated encoding that have not been previously considered, highlighting the importance of both theoretically and empirically driven

approaches in understanding brain-behavior relationships. More broadly, the work informs current theories on functional differentiations within the reward processing network and brings new evidence for the fruitfulness of utilizing individuals' connectivity patterns in the study of cognition (Finn et al., 2015; Gratton et al., 2018).

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

Abler, B., Walter, H., Erk, S., Kammerer, H., & Spitzer, M. (2006). Prediction error as a linear function of reward probability is coded in human nucleus accumbens. *NeuroImage*, 31(2), 790–795. https://doi.org/10.1016/j.neuroimage.2006.01.001

Adcock, R. A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., & Gabrieli, J. D. E. (2006). Reward-motivated learning: Mesolimbic activation precedes memory formation. *Neuron*, 50(3), 507–517. https://doi.org/10.1016/j.neuron.2006.03.036

Amiez, C., Joseph, J. P., & Procyk, E. (2006). Reward encoding in the monkey anterior cingulate cortex. *Cerebral Cortex*, 16(7), 1040–1055. https://doi.org/10.1093/cercor/bhj046

Bartra, O., McGuire, J. T., & Kable, J. W. (2013). The valuation system: A coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. *NeuroImage*, 76, 412–427. https://doi.org/10.1016/j.neuroimage.2013.02.063

Biallleck, K. A., Schaal, H.-P., Kranz, T. A., Fell, J., Elger, C. E., & Axmacher, N. (2011). Ventromedial prefrontal cortex activation is associated with memory formation for predictable rewards. *PLoS One*, 6(2), e16695. https://doi.org/10.1371/journal.pone.0016695

Blessing, E. M., Beissner, F., Schumann, A., Brünner, F., & Bär, K. J. (2016). A data-driven approach to mapping cortical and subcortical intrinsic functional connectivity along the longitudinal hippocampal axis. *Human Brain Mapping*, 37(2), 462–476. https://doi.org/10.1002/hbm.23042

Boorman, E. D., Behrens, T. E. J., Woolrich, M. W., & Rushworth, M. F. S. (2009). How green is the grass on the other side? Frontopolar cortex and the evidence in favor of alternative courses of action. *Neuron*, 62(5), 733–743. https://doi.org/10.1016/j.neuron.2009.05.014

Bowman, C.R. & Zeithamova, D. (2018). Abstract memory representations in the ventromedial prefrontal cortex and hippocampus support concept generalization. *Journal of Neuroscience, 38(10)*, 2605-2614

Brunec, I. K., Bellana, B., Ozubko, J. D., Man, V., Robin, J., Liu, Z. X., … Moscovitch, M. (2018). Multiple scales of representation along the hippocampal anteroposterior axis in humans. *Current Biology, 28*(13), 2129–2135.e6. https://doi.org/10.1016/j.cub.2018.05.016

Camara, E., Rodriguez-Fornells, A., & Münte, T. F. (2009). Functional connectivity of reward processing in the brain. *Frontiers in Human Neuroscience*, 2(19), 1–14. https://doi.org/10.3389/neuro.09.019.2008

Cao, W., Luo, C., Zhu, B., Zhang, D., Dong, L., Gong, J., … Yao, D. (2014). Resting-state functional connectivity in anterior cingulate cortex in normal aging. *Frontiers in Aging Neuroscience, 6*(OCT), 1–7. https://doi.org/10.3389/fnagi.2014.00280

Doll, B. B., Shohamy, D., & Daw, N. D. (2015). Multiple memory systems as substrates for multiple decision systems. *Neurobiology of Learning and Memory*, 117(9), 4–13. https://doi.org/10.1016/j.nlm.2014.04.014

Duncan, K., Tompary, A., & Davachi, L. (2014). Associative encoding and retrieval are predicted by functional connectivity in distinct hippocampal area CA1 pathways. *Journal of Neuroscience*, 34(34), 11188–98. https://doi.org/10.1523/JNEUROSCI.0521-14.2014

Elliott, R., Agnew, Z., & Deakin, J. F. W. (2008). Medial orbitofrontal cortex codes relative rather than absolute value of financial rewards in humans. *European Journal of Neuroscience*, 27(9), 2213–2218. https://doi.org/10.1111/j.1460-9568.2008.06202.x

Elliott, R., Newman, J. L., Longe, O. A., & Deakin, J. F. (2003). Differential response patterns in the striatum and orbitofrontal cortex to financial reward in humans: A parametric functional magnetic resonance imaging study. *Journal of Neuroscience*, 23(1), 303–307.

Finn, E. S., Shen, X., Scheinost, D., Rosenberg, M. D., Huang, J., Chun, M. M., … Constable, R. T. (2015). Functional connectome fingerprinting : identifying individuals using patterns of brain connectivity. *Nature Neuroscience, 18*(11), 1664–1671. https://doi.org/10.1038/nn.4135

Fiorillo, Christopher D, Tobler, P. N., & Schultz, W. (2003). Discrete coding of reward dopamine neurons. *Science*, 299(March), 1898–1902. https://doi.org/10.1126/science.1077349

Gerraty, R. T., Davidow, J. Y., Wimmer, G. E., Kahn, I., & Shohamy, D. (2014). Transfer of learning relates to intrinsic connectivity between hippocampus, ventromedial prefrontal cortex, and large-scale networks. *Journal of Neuroscience*, 34(34), 11297–11303. https://doi.org/10.1523/JNEUROSCI.0185-14.2014

Gluth, S., Sommer, T., Rieskamp, J., & Büchel, C. (2015). Effective connectivity between hippocampus and ventromedial prefrontal cortex controls preferential choices from memory. *Neuron*, 86(4), 1078–1090. https://doi.org/10.1016/j.neuron.2015.04.023

Gratton, C., Laumann, T. O., Nielsen, A. N., Greene, D. J., Gordon, E. M., Gilmore, A. W., … Petersen, S. E. (2018). Functional brain networks are dominated by stable group and individual factors, not cognitive or daily variation. *Neuron, 98*(2), 439–452.e5. https://doi.org/10.1016/j.neuron.2018.03.035

Gruber, M. J., Ritchey, M., Wang, S. F., Doss, M. K., & Ranganath, C. (2016). Post-learning hippocampal dynamics promote preferential retention of rewarding events. *Neuron*, 89(5), 1110–1120. https://doi.org/10.1016/j.neuron.2016.01.017

Hamann, J. M., Dayan, E., Hummel, F. C., & Cohen, L. G. (2014). Baseline frontostriatal-limbic connectivity predicts reward-based memory formation. *Human Brain Mapping*, 35(12), 5921–5931. https://doi.org/10.1002/hbm.22594

Hare, T. A., O'Doherty, J., Camerer, C. F., Schultz, W., & Rangel, A. (2008). Dissociating the role of the orbitofrontal cortex and the striatum in the computation of goal values and prediction errors. *Journal of Neuroscience*, 28(22), 5623–5630. https://doi.org/10.1523/JNEUROSCI.1309-08.2008

Honey, C. J., Sporns, O., Cammoun, L., Gigandet, X., Thiran, J. P., Meuli, R., & Hagmann, P. (2009). Predicting human resting-state functional connectivity from structural connectivity. *Proceedings of the National Academy of Sciences*, 106(6), 2035–2040. https://doi.org/10.1073/pnas.0811168106

Kable, J. W., & Glimcher, P. W. (2007). The neural correlates of subjective value during intertemporal choice. *Nature Neuroscience*, 10(12), 1625–1633. https://doi.org/10.1038/nn2007

Kafkas, A., & Montaldi, D. (2015). Striatal and midbrain connectivity with the hippocampus selectively boosts memory for contextual novelty. *Hippocampus*, 25(11), 1262–1273. https://doi.org/10.1002/hipo.22434

Kahn, I., & Shohamy, D. (2013). Intrinsic connectivity between the hippocampus, nucleus accumbens, and ventral tegmental area in

humans. *Hippocampus*, *23*(3), 187–192. https://doi.org/10.1002/hipo.22077

Kaping, D., Vinck, M., Hutchison, R. M., Everling, S., & Womelsdorf, T. (2011). Specific contributions of ventromedial, anterior cingulate, and lateral prefrontal cortex for attentional selection and stimulus valuation. *PLoS Biology*, *9*(12). https://doi.org/10.1371/journal.pbio.1001224

Knutson, B., Taylor, J., Kaufman, M., Peterson, R., & Glover, G. (2005). Distributed Neural representation of expected value. *Journal of Neuroscience*, *25*(19), 4806–4812. https://doi.org/10.1523/JNEUROSCI.0642-05.2005

Lisman, J., Grace, A. A., & Duzel, E. (2011). A neoHebbian framework for episodic memory; role of dopamine-dependent late LTP. *Trends in Neurosciences*, *34*(10), 536–547. https://doi.org/10.1016/j.tins.2011.07.006

Lisman, J. E., & Grace, A. A. (2005). The hippocampal-VTA loop: Controlling the entry of information into long-term memory. *Neuron*, *46*(5), 703–713. https://doi.org/10.1016/j.neuron.2005.05.002

Luk, C.-H., & Wallis, J. D. (2013). Choice coding in frontal cortex during stimulus-guided or action-guided decision-making. *Journal of Neuroscience*, *33*(5), 1864–1871. https://doi.org/10.1523/JNEUROSCI.4920-12.2013

Margulies, D. S., Kelly, A. M. C., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *NeuroImage*, *37*(2), 579–588. https://doi.org/10.1016/j.neuroimage.2007.05.019

McKenzie, S., Frank, A. J., Kinsky, N. R., Porter, B., Rivière, P. D., & Eichenbaum, H. (2014). Hippocampal representation of related and opposing memories develop within distinct, hierarchically organized neural schemas. *Neuron*, *83*(1), 202–215. https://doi.org/10.1016/j.neuron.2014.05.019

Meyer, D., Dimitriadou, E., Hornik, K., Weingessel A., & Leisch, F. (2017). e1071: Misc Functions of the Department of Statistics, Probability Theory Group (Formerly: E1071), TU Wien. R package version 1.6-8. https://CRAN.R-project.org/package=e1071

Miendlarzewska, E. A., Bavelier, D., & Schwartz, S. (2016). Influence of reward motivation on human declarative memory. *Neuroscience and Biobehavioral Reviews*, *61*, 156–176. https://doi.org/10.1016/j.neubiorev.2015.11.015

Montague, P., Dayan, P., & Sejnowski, T. (1996). A framework for mesencephalic dopamine systems based on predictive Hebbian learning. *The Journal of Neuroscience*, *16*(5), 1936–1947. https://doi.org/10.1523/JNEUROSCI.16-05-01936.1996

Murphy, K., Birn, R. M., & Bandettini, P. A. (2013). Resting-state fMRI confounds and cleanup. *NeuroImage*, *80*(4), 349–359. https://doi.org/10.1016/j.neuroimage.2013.04.001

Murty, V. P., LaBar, K. S., & Adcock, R. A. (2016). Distinct medial temporal networks encode surprise during motivation by reward versus punishment. *Neurobiology of Learning and Memory*, *134*, 55–64. https://doi.org/10.1016/j.nlm.2016.01.018

Murty, V. P., Tompary, A., Adcock, R. A., & Davachi, L. (2017). Selectivity in postencoding connectivity with high-level visual cortex is associated with reward-motivated memory. *The Journal of Neuroscience*, *37*(3), 537–545. https://doi.org/10.1523/JNEUROSCI.4032-15.2017

Newton, A., Morgan, V., Rogers, B., & Gore, J. (2011). Modulation of steady state functional connectivity in the default mode and working memory networks by cognitive load. *Human Brain Mapping*, *32*(10), 1649–1659. https://doi.org/10.1002/hbm.21138.Modulation

Nieuwenhuis, I. L. C., & Takashima, A. (2011). The role of the ventromedial prefrontal cortex in memory consolidation. *Behavioural Brain Research*, *218*(2), 325–334. https://doi.org/10.1016/j.bbr.2010.12.009

O'Doherty, J. P. (2011). Contributions of the ventromedial prefrontal cortex to goal-directed action selection. *Annals of the New York Academy of Sciences*, *1239*(1), 118–129. https://doi.org/10.1111/j.1749-6632.2011.06290.x

Patil, A., Murty, V. P., Dunsmoor, J. E., Phelps, E. A., & Davachi, L. (2017). Reward retroactively enhances memory consolidation for related items. *Learning and Memory*, *24*(1), 65–69. https://doi.org/10.1101/lm.042978.116

Poole, V. N., Robinson, M. E., Singleton, O., DeGutis, J., Milberg, W. P., McGlinchey, R. E., … Esterman, M. (2016). Intrinsic functional connectivity predicts individual differences in distractibility. *Neuropsychologia, 86,* 176–182. https://doi.org/10.1016/j.neuropsychologia.2016.04.023

Poppenk, J., Evensmoen, H. R., Moscovitch, M., & Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends in Cognitive Sciences*, *17*(5), 230–240. https://doi.org/10.1016/j.tics.2013.03.005

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, *59*(3), 2142–2154. https://doi.org/10.1016/j.neuroimage.2011.10.018

Ranganath, C., Heller, A., Cohen, M. X., Brozinsky, C. J., & Rissman, J. (2005). Functional connectivity with the hippocampus during successful memory formation. *Hippocampus*, *15*(8), 997–1005. https://doi.org/10.1002/hipo.20141

Rissman, J., Gazzaley, A., & D'Esposito, M. (2004). Measuring functional connectivity during distinct stages of a cognitive task. *NeuroImage*, *23*(2), 752–763. https://doi.org/10.1016/j.neuroimage.2004.06.035

Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., & Smith, S. M. (2004). Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry*, *55*(6), 594–602. https://doi.org/10.1016/j.biopsych.2003.11.012

Salvador, R., Suckling, J., Coleman, M. R., Pickard, J. D., Menon, D., & Bullmore, E. (2005). Neurophysiological architecture of functional magnetic resonance images of human brain. *Cerebral Cortex*, *15*(9), 1332–2342. https://doi.org/10.1093/cercor/bhi016

Seymour, B., & McClure, S. M. (2008). Anchors, scales and the relative coding of value in the brain. *Current Opinion in Neurobiology*, *18*(2), 173–178. https://doi.org/10.1016/j.conb.2008.07.010

Shigemune, Y., Tsukiura, T., Kambara, T., & Kawashima, R. (2014). Remembering with gains and losses: Effects of monetary reward and punishment on successful encoding activation of source memories. *Cerebral Cortex*, *24*(5), 1319–1331. https://doi.org/10.1093/cercor/bhs415

Shohamy, D., & Adcock, R. A. (2010). Dopamine and adaptive memory. *Trends in Cognitive Sciences*, *14*(10), 464–472. https://doi.org/10.1016/j.tics.2010.08.002

Silvetti, M., Seurinck, R., & Verguts, T. (2011). Value and prediction error in medial frontal cortex: Integrating the single-unit and systems levels of analysis. *Frontiers in Human Neuroscience*, *5*(August), 1–15. https://doi.org/10.3389/fnhum.2011.00075

Squire, L. R. (1992). Probabilistic similarity search for uncertain time series. *Psychological Review*, *99*(2), 195–231.

Strait, C. E., Blanchard, T. C., & Hayden, B. Y. (2014). Reward value comparison via mutual inhibition in ventromedial prefrontal cortex. *Neuron*, *82*(6), 1357–1366. https://doi.org/10.1016/j.neuron.2014.04.032

Tambini, A., Ketz, N., & Davachi, L. (2010). Enhanced brain correlations during rest are related to memory for recent experiences. *Neuron*, *65*(2), 280–290. https://doi.org/10.1016/j.neuron.2010.01.001

Tambini, A., Rimmele, U., Phelps, E. A., & Davachi, L. (2016). Emotional brain states carry over and enhance future memory formation. *Nature Neuroscience*, *20*(2), 271–278. https://doi.org/10.1038/nn.4468

Tobler, P. N., Fiorillo, C. D., & Schultz, W. (2005). Adaptive coding of reward value by dopamine neurons. *Science*, *307*(5715), 1642–1645. https://doi.org/10.1126/science.1105370

Tompary, A., Duncan, K., & Davachi, L. (2015). Consolidation of associative and item memory is related to post-encoding functional connectivity between the ventral tegmental area and different medial temporal lobe subregions during an unrelated task. *Journal of Neuroscience*, *35*(19), 7326–7331. https://doi.org/10.1523/JNEUROSCI.4816-14.2015

Touroutoglou, A., Andreano, J. M., Barrett, L. F., & Dickerson, B. C. (2015). Brain network connectivity-behavioral relationships exhibit trait-like properties: Evidence from hippocampal connectivity and memory. *Hippocampus*, *25*(12), 1591–1598. https://doi.org/10.1002/hipo.22480

Tsukiura, T., & Cabeza, R. (2008). Orbitofrontal and hippocampal contributions to memory for face-name associations: The rewarding power of a smile. *Neuropsychologia*, *46*(9), 2310–2319. https://doi.org/10.1016/j.neuropsychologia.2008.03.013

Tversky, A., & Kahneman, D. (1981). The framing of decisions and the psychology of choice. *Science*, *211*, 453–458.

Urner, M., Schwarzkopf, D. S., Friston, K., & Rees, G. (2013). Early visual learning induces long-lasting connectivity changes during rest in the human brain. *NeuroImage*, *77*, 148–156. https://doi.org/10.1016/j.neuroimage.2013.03.020

Van Dijk, K. R. A., Hedden, T., Venkataraman, A., Evans, K. C., Lazar, S. W., & Buckner, R. L. (2010). Intrinsic functional connectivity as a tool for human connectomics: theory, properties, and optimization. *Journal of Neurophysiology*, *103*(1), 297–321. https://doi.org/10.1152/jn.00783.2009

Walton, M. E., Chau, B. K. H., & Kennerley, S. W. (2015). Prioritising the relevant information for learning and decision making within orbital and ventromedial prefrontal cortex. *Current Opinion in Behavioral Sciences*, *1*, 78–85. https://doi.org/10.1016/j.cobeha.2014.10.005

Wang, L., Negreira, A., LaViolette, P., Bakkour, A., Sperling, R. A, & Dickerson, B. C. (2010). Intrinsic interhemispheric hippocampal functional connectity predicts indivual differences in memory performance ability. *Hippocampus*, *20*(3), 345–351. https://doi.org/10.1002/hipo.20771.Intrinsic

Wang, S. H., Tse, D., & Morris, R. G. M. (2012). Anterior cingulate cortex in schema assimilation and expression. *Learning and Memory*, *19*(8), 315–318. https://doi.org/10.1101/lm.026336.112

Weible, A. P., Rowland, D. C., Monaghan, C. K., Wolfgang, N. T., & Kentros, C. G. (2012). Neural correlates of long-term object memory in the mouse anterior cingulate cortex. *Journal of Neuroscience*, *32*(16), 5598–5608. https://doi.org/10.1523/JNEUROSCI.5265-11.2012

Wimmer, G. E., Daw, N. D., & Shohamy, D. (2012). Generalization of value in reinforcement learning by humans. *European Journal of Neuroscience*, *35*(7), 1092–1104. https://doi.org/10.1111/j.1460-9568.2012.08017.x

Wittmann, B. C., Schott, B. H., Guderian, S., Frey, J. U., Heinze, H. J., & Düzel, E. (2005). Reward-related fMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. *Neuron*, *45*(3), 459–467. https://doi.org/10.1016/j.neuron.2005.01.010

Wolosin, S. M., Zeithamova, D., & Preston, A. R. (2012). Reward modulation of hippocampal subfield activation during successful associative encoding and retrieval. *Journal of Cognitive Neuroscience*, *24*(7), 1532–1547. https://doi.org/10.1162/jocn_a_00237

Wolosin, S. M., Zeithamova, D., & Preston, A. R. (2013). Distributed hippocampal patterns that discriminate reward context are associated with enhanced associative binding. *Journal of Experimental Psychology*, *142*(4), 1264–1276. https://doi.org/10.1037/a0033609

Yan, C., Su, L., Wang, Y., Xu, T., Yin, D., Fan, M., … Chan, R. C. K. (2016). Multivariate neural representations of value during reward anticipation and consummation in the human orbitofrontal cortex. *6*, 29079. https://doi.org/10.1038/srep29079

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods*, *8*(8), 665–670. https://doi.org/10.1038/nmeth.1635

Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and ventral medial prefrontal activation during retrieval-mediated learning supports novel inference. *Neuron*, *75*(1), 168–179. https://doi.org/10.1016/j.neuron.2012.05.010

Zeithamova, D., Gelman, B. D., Frank, L., & Preston, A. R. (2018). Abstract representation of prospective reward in the hippocampus. *The Journal of Neuroscience*, *38*(Xx), 0719-18. https://doi.org/10.1523/JNEUROSCI.0719-18.2018

Zeithamova, D., Manthuruthil, C., & Preston, A. R. (2016). Repetition suppression in the medial temporal lobe and midbrain is altered by event overlap. *1477*(August), 1464–1477. https://doi.org/10.1002/hipo.22622