Published in final edited form as:

Hippocampus. 2016 September ; 26(9): 1168–1178. doi:10.1002/hipo.22598.

Reactivation during encoding supports the later discrimination of similar episodic memories

Rebecca N. van den Honert¹, Gregory McCarthy^{1,2}, and Marcia K. Johnson^{1,2}

¹ Department of Psychology, Yale University, New Haven, CT, USA

² Interdepartmental Neuroscience Program, Yale University, New Haven, CT, USA

Abstract

Episodic memory is characterized by remembering events as unique combinations of features. Even when some features of events overlap, we are later often able to discriminate among them. Here we ask whether hippocampally mediated *reactivation* of an earlier event when a similar one occurs supports subsequent memory that two similar but not identical events occurred (mnemonic discrimination). In two experiments, participants viewed objects (Experiment 1) or scenes (Experiment 2) during functional MRI (fMRI). After scanning, participants had to remember whether repeated items had been identical or similar. In Experiment 2, representational similarity between the 1st and 2nd presentation predicted participants' ability to remember that the presentations were different, suggesting that the first item was reactivated while viewing the second. A similar but weaker result was found in Experiment 1 that did not survive correction for multiple comparisons. Furthermore, both experiments yielded evidence that the hippocampus was involved in reactivation; hippocampal pattern similarity (and, in Experiment 2, hippocampal activity during the 2nd presentation) correlated with pattern similarity in several regions of visual cortex. These results provide the first fMRI evidence that hippocampus-mediated reactivation contributes to the later memory that two similar, but different events occurred.

Keywords

pattern completion; reminding; source memory; study-phase; retrieval

Introduction

The features of our experiences (e.g., color, shape, sound, time, place, emotion) cohere to form memories with an episodic quality (Underwood, 1969; Tulving, 1972; Johnson, Hashtroudi & Lindsay, 1993). Events with overlapping features are likely to be confused during remembering (Underwood, 1969; Johnson et al., 1993), and experiences that are encoded in a way that preserves their differences are less likely to be confused. Despite the centrality of this issue for understanding episodic memory, the encoding mechanisms for such *mnemonic discrimination* are not well understood.

Here we investigate a possible mechanism for increasing the chances of mnemonic discrimination – hippocampally mediated *reactivation* (Johnson & Chalfonte, 1994; Norman & O'Reilly, 2003; Ranganath, 2010). Reactivation of a previous event provides an opportunity for participants to notice and encode that a similar, but not identical, event occurred before, which could then be the basis of later remembering that two similar events occurred.

There is considerable behavioral evidence that reactivation of an item or event increases the likelihood that it will be subsequently remembered. This can be seen in the benefits of testing (Roediger & Karpicke, 2006), including memory for the features of events (Henkel, 2004). Reactivation may be particularly helpful in preserving a memory in the face of interfering information. Retroactive interference can be reduced when A-B is remembered while learning A-C (Postman & Parker, 1970). This could explain why retroactive interference paradigms that use related paired associates (A-B, A-B' instead of the typical A-B, A-C) find improved memory for A-B, instead of interference (Barnes & Underwood, 1959); B' may cue reactivation of B during the encoding of A-B'. Reactivation not only strengthens the reactivated memory trace, but also can beneficially affect how a potentially competing memory is encoded. A recent study showed that detecting and remembering the difference between A-B and A-C while studying A-C facilitated the subsequent cued recall of C (Wahlheim & Jacoby, 2013). More generally, it has been proposed that reminders of one event by another could help explain the basis of frequency or recency judgments of repetitions of the same event (Hintzman, 2004) or judgments of the temporal order of related events (Hintzman, 2010).

The hippocampus (HC) plays a key role in reactivation. HC activity during a memory test is associated with successful recall (Eldridge et al., 2000), including recall of event features (Giovanello, Schnyer, & Verfaellie, 2004), and with neural measures of representational similarity between study and test (Gordon, Rissman, Kiani, & Wagner, 2013; Ritchey, Wing, LaBar, & Cabeza, 2013; Bosch, Jehee, Fernández, & Doeller, 2014; Staresina, Henson, Kriegeskorte, & Alink, 2012; Wing, Ritchey, & Cabeza, 2015). Although such studies demonstrate that remembering involved HC-based reactivation, they do not link HC-based reactivation to *subsequent* memory.

A beneficial effect of reactivation on subsequent memory is implied but not demonstrated, when greater neural pattern similarity across repetitions of an item is associated with subsequent recognition memory of that item (Ward, Chun, & Kuhl, 2013; Xue et al., 2010; 2013; Lu, Wang, Chen, & Xue, 2015). Although this finding could reflect the impact of reactivation on subsequent memory, it could instead reflect the impact of consistent encoding during repeated exposures to the same stimulus. More direct evidence regarding the benefits of HC-based reactivation for subsequent memory comes from a study using an A-B, A-C interference paradigm. After participants studied A-B, the hippocampus was more active while studying A-C if B was later remembered than if B was forgotten (Kuhl, Shah, DuBrow, & Wagner, 2010).

Attributing brain activity to reactivation is complicated by the fact that encoding and reactivation are temporally intertwined during ongoing cognition. The hippocampus is

known to play a role in encoding (e.g., binding features within events) as well as reactivation (Davachi, 2006; Eichenbaum, Yonelinas & Ranganath, 2007; Norman, 2010). Thus hippocampal activity during a second event could reflect its role in specific, distinct encoding of that event without reference to an earlier event.

One study attempted to demonstrate that hippocampal activity during an interference paradigm reflects *reactivation* of a previous event rather than distinct encoding of a second event. Using an A-B, A-C interference paradigm, Kuhl et al. (2010) presented participants with overlapping pairs of objects (e.g. *watch-sink*, and then *watch-pipe*). After scanning, memory for B was tested (e.g., *watch-s_____*). During learning, each object pair was associated with a monetary reward (high or low). Hippocampal activity during A-C learning positively related to subsequent memory for B, implying that hippocampal processing during A-C learning protects from retroactive interference. To differentiate between hippocampal-based reactivation of A-B and hippocampal-based distinct encoding of A-C, Kuhl et al. (2010) computed an indirect measure of A-B reactivation during A-C learning. Activity in reward-related regions during A-C encoding did not relate to the level of reward for A-C, but instead with A-B's level of reward, suggesting that reactivation of the reward-context of A-B while learning A-C.

In summary, there is strong evidence that reactivation improves memory for a single event and that the hippocampus is responsible for reactivation. However, there is limited direct evidence that hippocampal-based reactivation during encoding supports the future discrimination of two similar events, that is, mnemonic discrimination.¹ A direct demonstration of this requires a) evidence of reactivation b) evidence that the HC is responsible for that reactivation, and c) evidence that reactivation improves subsequent memory that two different events occurred. Here we used a paradigm and analysis protocol that allowed us to measure all three of these elements.

If reactivation is playing a role in subsequent mnemonic discrimination, then high values of representational similarity between two similar events should be correlated with subsequent memory (i.e., a reactivation hypothesis). If subsequent memory that two different events occurred depends primarily on the difference between how they were encoded (i.e., a distinct encoding hypothesis), then we would expect that lower values of representational similarity between two similar events would be correlated with subsequent memory.

In two experiments, participants viewed objects (Exp. 1) or scenes (Exp. 2) that were shown once, repeated identically, or repeated as a similar version. Later, participants were shown word cues (e.g., *Anchor*) and had to remember whether or not they saw two identical or two similar versions (similar to Manelis et al., 2013). We then related the representational similarity during encoding of each *similar* object pair to participants' later memory for the objects as identical or different.

¹The task used here is a type of source memory task, but since we did not ask explicitly for source information (e.g., was the baseball glove on the left or right, or what color was the t-shirt?), but only whether participants remembered two items as the same or different, we use the relatively neutral term mnemonic discrimination. Note that this term has been used in the past to refer to discriminating between a previously seen stimulus and a perceptually present stimulus (e.g., Yassa & Stark, 2011).

A second experiment was designed to improve sensitivity of the task over the procedure used in the first experiment. In Experiment 2, participants were shown scenes instead of objects. Based on prior findings, scene stimuli should be particularly likely to engage the hippocampus (Zeidman, Mullally, & Maguire, 2015). Experiment 2 also had a longer inter-trial interval and slice acquisition was aligned with the long axis of the hippocampus. Stimulus pairs were also more similar in Experiment 2 – scene repeats only varied in terms of whether they were shown in full color or in gray scale. Using highly similar pairs should make it easier to detect evidence of reactivation. Given the anatomical overlap between perceptual and mnemonic representations (Chun & Johnson, 2011), reactivation may be hard to detect if relatively large perceptual differences wash out any similarity caused by reactivation.

Method

Participants

Participants were members of the Yale/New Haven community who gave written, informed consent in accordance with the Yale Human Investigations Committee. All participants had normal or corrected-to-normal vision and no history of neurological or psychiatric illness. Experiment 1 had 25 participants (13 females, mean age = 22.4 ± 4.9 years) and Experiment 2 had 24 participants (15 females, mean age = 22.5 ± 3.8 years). Data from 6 additional participants in Experiment 1, and from 4 additional participants in Experiment 2, were excluded for movement (3 in Exp. 1; 3 in Exp. 2), technical difficulties during scanning (2 in Exp. 1; 1 in Exp. 2), or an extremely low response rate in the fMRI (1 in Exp. 1; 0 in Exp. 2). Excessive movement was defined as having more than 50 TRs for which the Euclidean norm of the motion derivative exceeded 1.0.

Incidental Encoding Task

During fMRI, participants viewed objects one at a time (duration = 1 second, ISI = 2, 4, or 6 seconds) and were asked to indicate whether or not they would be likely to encounter the object in a typical week (Figure 1, left). Stimuli consisted of 600 photos of nameable objects collected from the 934 pictures used by Brady, Konkle, Alvarez, & Oliva (2008) (MIT Massive Memory set) and from Google image searches. All stimuli were color photographs centered on a white background. The set of pictures was divided into 300 pairs of items. Each participant saw 250 objects while in the scanner: 50 objects were shown only one time (single), 100 were shown twice (identical repetition), and 100 were two objects with the same label (exemplar repetition). The remaining 50 objects were never shown as pictures, but their labels were used as lures in the subsequent memory test. Object assignment to each condition (Single presentation, Identical repetition, Exemplar repetition, and Lure) was counterbalanced across participants. Objects were presented in a pseudo random order such that repetitions were from 10 to 60 trials apart.

Experiment 2 was similar except for the following differences. Participants judged the aesthetic quality of each picture (Figure 1, right). Stimuli were 240 scenes that were either full color or gray scale (80 repeated identically, 80 repeated with a change in format (color or gray scale), 40 shown just once, and 40 reserved to be lures on the subsequent memory

test). Scenes were taken from a number of sources, mostly freely available pictures from the Internet. During the incidental encoding task, a label preceded scenes for 1 second, the scene was then shown for 2.5 seconds, followed by a fixation cross (ITI = 2.0, 3.5, or 5.0 seconds; ISI = 5.5, 7.0, 8.5 seconds).

Memory Test

Approximately 5-10 minutes after scanning, participants completed a surprise recognition memory test. Most participants did not suspect a memory test, and no participants suspected any specific type of test. They were shown word cues (e.g., *baseball glove*, *baseball park*) representing objects/scenes they might have seen while in the scanner. For each word, they had to indicate whether they had seen the associated picture 0 times, 1 time, as 2 identically repeated images, or as 2 different versions of the object/scene. Word cues were presented on a computer and participants responded by pressing one of four keys labeled *0*, *1*, *S* (for “Twice-Identical”), or *D* (for “Twice-Different”). The memory test was self-paced (ITI = 500ms) with a limit of up to 3s to respond (6s in Experiment 2).

Behavioral Analysis

Word cues on the memory test fell into one of four Presentation conditions: lure, single presentation, identical repetition, and exemplar repetition. Participants’ response options to the question of how often they saw each picture reflected these four possibilities (“Zero” times, “Once,” “Twice-Identical,” and “Twice-Different”). To assess participants’ performance, we conducted a 1-way repeated measures ANOVA (four levels of Response) for each Presentation condition, and then did planned comparisons of the correct response to all other responses. This analysis was conducted separately for Experiments 1 and 2.

fMRI Acquisition

Data were acquired using a Siemens Trio TIM 3.0T scanner and a 32-channel head coil. Functional images were collected using multi-band echo planar imaging [parameters: repetition time (TR) = 2,000ms, echo time (TE) = 32ms, flip angle $\alpha = 62^\circ$, field of view (FOV) = 200mm, matrix = 100^2 , slice thickness = 2mm, 60 slices, multi-band factor = 3]. High-resolution images were acquired using a 3D MP-RAGE sequence (TR = 2530ms, TE = 2.77ms, flip angle $\alpha = 7^\circ$, FOV = 256mm, matrix = 256^2 , slice thickness = 1mm, 176 slices). Data for Experiment 2 were acquired using the same parameters except that for the functional scans, there were 69 slices aligned with the long-axis of the HC and a matrix of 100×104 .

Preprocessing of fMRI Data

fMRI data were analyzed using the AFNI software package (<http://afni.nimh.nih.gov/afni>). The first 3 volumes (6s; 4 volumes, 8s, in Experiment 2) of each functional dataset were discarded to allow for MR equilibration. Motion correction and normalization were completed with a single transformation: functional volumes were aligned to each other and to each individual's high-resolution anatomical scan in one transformation. Data were not spatially smoothed. Each voxel's time series was scaled (within runs) to a mean of 100 and a maximum of 200 to allow betas to more closely reflect percent signal change.

Regions of interest were defined using FreeSurfer's automatic volumetric segmentation (<http://surfer.nmr.mgh.harvard.edu/>) with a probability threshold of 50% (Figure 2). We defined 5 anatomical ROIs in occipitotemporal cortex and medial temporal lobe: lateral occipital cortex (LOC), fusiform cortex (FUS), parahippocampal cortex (PHC), entorhinal cortex (ERC), and HC. The same five anatomical areas were analyzed in both experiments for consistency; however, LOC was chosen because of its object sensitivity and objects were presented in Experiment 1 (Malach et al., 1995) and the fusiform was chosen because it contains color-sensitive voxels and color was manipulated in Experiment 2 (Damasio, Yamada, Damasio, Corbett, & McKee, 1980; Pearlman, Birch, & Meadows, 1979; Zeki, 1990; Grill-Spector, Malach, 2004). All ROIs were bilateral. Custom Matlab scripts filled very small gaps in the automatic FreeSurfer ROIs, and visual inspection with minor manual edits ensured precise anatomical coverage. Voxels at the border of two ROIs that were assigned to both (e.g., PHC and HC) were excluded from the analysis.

Measuring Pattern Similarity and Repetition Suppression

We used two measures of representational similarity commonly used in fMRI – pattern similarity and repetition suppression. Pattern similarity measures the correlation (or Euclidean distance, etc.) between the voxel pattern elicited by one stimulus and that elicited by another stimulus (for review of this and other multi-voxel pattern analyses, see (Norman, Polyn, & Detre, 2006). High correlations suggest that a region represents two stimuli in a similar way, whereas relatively low correlations suggest the region either contains information that distinguishes the two stimuli, or does not represent information about the features of the stimuli at all. Repetition suppression refers to the lower BOLD response in a region to a stimulus upon a second presentation compared to the first (Epstein et al., 2008). How exactly to interpret repetition suppression is debated (see Davis & Poldrack, 2013), but it is often used to index how similarly a region either processes or represents two stimuli (e.g., Bakker et al., 2008; Lacy et al., 2011). Pattern similarity is more commonly used in investigations relating perceptual vs. reflective representations, including studies of reactivation (e.g., Kuhl & Chun, 2014; Kuhl et al., 2012). Given the possibility that pattern similarity and repetition suppression may be differentially associated with different aspects of memory (e.g., explicit vs. implicit memory, Ward et al., 2013), we report both measures here.

In order to obtain a multi-voxel pattern of activity for each trial in each region, we modeled individual trials using AFNI's 3dREML. The resulting betas were then z-scored across trials within each voxel. Voxels with average activity ± 5 standard deviations away from the mean were excluded from the analysis. The normalized betas within an ROI form pairs of vectors for each of the two presentations of a picture. These two vectors were correlated and the resulting r -value was Fisher z' – transformed to obtain a pattern similarity score for each object pair (Exp 1) or scene pair (Exp 2). Thus, a high pattern similarity score indicates a region exhibited a similar pattern of brain activity during the 1st and 2nd presentation of an object or scene.

To parallel our pattern similarity approach, single trial estimates were also used to calculate repetition suppression. For each critical pair we took the average 1st presentation beta, across

voxels in the ROI, and subtracted the average 2nd presentation beta across voxels. A high value of repetition suppression indicates a region is insensitive to the variation across 1st and 2nd presentation, that is, that the region represents the two similarly.

Relating Neural Measures of Representational Similarity to Subsequent Memory

To determine if pattern similarity/repetition suppression in any particular region related to memory, we conducted linear mixed-effects logistic regressions using the `glmer` function in the `lme4` package (Bates, Maechler, Bolker, & Walker, 2013) in R (R Core Team, 2015). We predicted Response (“Twice-Identical” or “Twice-Different”) using pattern similarity/repetition suppression in the ROI. Subjects were included as a random factor such that the intercept for each subject could vary. Two additional nuisance predictors were included in each model – the trial lag between repeats and overall BOLD activity (averaged across the two presentations). We included lag because pattern similarity, repetition suppression, and subsequent memory can be affected by the lag between repetitions (Ward et al., 2013). Similarly, increased attention might result in improved memory as well as higher overall BOLD activity, which, in turn, improves signal-to-noise and results in higher pattern similarity or repetition suppression (LaRocque et al., 2013). All reported p-values have been adjusted to correct for multiple comparisons (5 ROIs), by limiting the false-discovery rate to be below 0.05 (Benjamini & Hochberg, 1995).

We limited our analysis to Exemplar pairs because our hypotheses are not testable for Identical pairs. We may find that Exemplar pairs correctly called “Twice-Different” have higher or lower pattern similarity than those called “Twice-Identical.” The former would suggest reactivation while the latter would suggest distinct encodings. In contrast, if we found that Identical pairs correctly called “Twice-Identical” had higher representational similarity than those incorrectly called “Twice-Different” it would be unclear whether that was due to perceptual similarity or the perceptual-reflective representational similarity caused by reactivation. Nonetheless, we include the results of analyses using Identical pairs parallel to the Exemplar pair analyses (Supplemental Material).

The product of hippocampal reactivation may manifest in representational regions. For example, one study of episodic reinstatement during remembering found greater encoding-retrieval pattern similarity for remembered than forgotten word-scene pairs in parahippocampal cortex but not in the HC (Staresina et al., 2012). Interestingly, hippocampal *activity* during remembering correlated with the extent of encoding-retrieval similarity in parahippocampal cortex. To allow for this possibility we correlated hippocampal activity on the 2nd presentation of an item with pattern similarity in each ther ROI. The resulting r-values were Fisher Z’ – transformed and then tested against zero with a one-sample t-test.

Results

Behavioral Results

Figure 3 shows participants’ average rate of responding “Zero,” “Once,” “Twice-Identical” and “Twice-Different” in each of the Presentation conditions (Lure, Single Item, Identical

Repetition, and Exemplar Repetition) for Experiments 1 and 2. In Experiment 1, each of the four 1-way ANOVAs within presentation condition revealed a significant main effect of Response, all $F(3,75) > 128$, all p 's < 0.001 . Planned subsequent comparisons indicated that the correct response was always significantly more likely than the incorrect responses (all Bonferroni corrected p 's < 0.001). Experiment 2 yielded similar results. Each of the four 1-way ANOVAs within presentation condition revealed a significant main effect of Response (all p 's < 0.001). Planned subsequent comparisons indicated that the correct response was always significantly more likely than the incorrect responses (all Bonferroni corrected p 's < 0.001).

Logistic Regression Results

Figure 4 shows the expected logistic regressions from the reactivation (blue) and distinct encoding (red) perspectives. For convenience, the y-axis is labeled P("Twice-Different") or the probability of a correct response. Figures 5 and 6 depict fitted logistic curves using pattern similarity and repetition suppression as predictors, respectively.

First, did multi-voxel pattern similarity relate to participants' subsequent memory for differences? In Experiment 1, pattern similarity in FUS participants' memory for differences ($B=1.44$, $SE=0.72$, uncorrected $p<0.05$, corrected $p>0.10$; top, Figure 5). In Experiment 2, high pattern similarity in LOC, FUS, PHC, and HC predicted participants' memory for differences (LOC: $B=1.47$, $SE=0.62$, $p<0.05$; FUS: $B=2.15$, $SE=1.03$, $p<0.05$; PHC: $B=1.66$, $SE=0.80$, $p<0.05$; HC: $B=1.92$, $SE=0.92$, $p<0.05$; bottom, Figure 5). Note that in Experiment 2, the trial lag between repeats was associated with higher memory performance but lower pattern similarity and therefore cannot be driving these effects (Tables S1 and S2).

Did repetition suppression relate to participants' subsequent memory for differences? In Experiment 1, repetition suppression did not significantly predict memory for differences; however *low* repetition suppression in LOC marginally predicted participants' memory for differences ($B=-0.27$, $SE=0.14$, uncorrected $p<0.05$, corrected $p>0.10$; top, Figure 6). In Experiment 2, we found some support for the reactivation-based prediction. *High* repetition suppression in the HC marginally predicted participants' memory for differences ($B=1.11$, $SE=0.44$, $p<0.06$; bottom, Figure 6).

In short, in Experiment 2, there was clear support for reactivation-based mnemonic discrimination using pattern similarity as an index of representational similarity.

Further specifying the role of the hippocampus (HC)

If reactivation in the HC contributes to pattern similarity in visual cortex, then hippocampal pattern similarity and/or activity should correlate with pattern similarity in visual cortex. In Experiment 1, HC pattern similarity correlated positively with pattern similarity in ERC (mean within participant $r = 0.71$; $t(24) = 31.9$, $p < 0.001$), PHC ($r = 0.84$; $t(24) = 25.1$, $p < 0.001$), FUS ($r = 0.77$; $t(24) = 22.0$, $p < 0.001$), and LOC ($r = 0.53$; $t(24) = 16.2$, $p < 0.001$). Likewise, in Experiment 2, HC pattern similarity correlated positively with pattern similarity in ERC ($r = 0.77$; $t(23) = 31.5$, $p < 0.001$), PHC ($r = 0.87$; $t(23) = 29.7$, $p < 0.001$), FUS ($r = 0.86$; $t(23) = 28.7$, $p < 0.001$), and LOC ($r = 0.54$; $t(23) = 17.4$, $p < 0.001$).

We also tested whether overall hippocampal activity during the 2nd exemplar related to pattern similarity elsewhere. In Experiment 1, HC activity during the 2nd presentation of an exemplar did not correlate with pattern similarity between 1st and 2nd presentations of exemplars in any ROI (all p 's > 0.10). However, in Experiment 2, HC activity during the 2nd presentation of an exemplar correlated positively with pattern similarity in the LOC (mean within participant $r = 0.05$; $t(23) = 2.12$, $p < 0.05$), FUS ($r = 0.10$; $t(23) = 3.20$, $p < 0.01$), ERC ($r = 0.05$; $t(23) = 2.24$, $p < 0.05$), and marginally in PHC ($r = 0.06$; $t(23) = 1.84$, $p < 0.10$).

Thus, pattern similarity in the HC between two similar events was positively correlated with pattern similarity in other regions (Experiments 1 and 2) and there was also evidence that level of activity in the HC during the processing of the 2nd exemplar was positively correlated with pattern similarity in other regions (Experiment 2). These findings are consistent with the idea that, especially in Experiment 2, the HC supported the reactivation of the 1st presentation while encoding the 2nd presentation.

It should be noted that both of these analyses collapsed across Response condition within exemplar pairs. In both experiments these correlations were significant when calculated separately for correct and incorrect pairs, but were not significantly greater for correct than incorrect pairs. We think this is consistent with hippocampal-based reactivation supporting mnemonic discrimination. Hippocampal pattern similarity/activity and visual cortex pattern similarity may be correlated even at lower levels of pattern similarity associated with incorrect responses.

Discussion

A fundamental characteristic of episodic memory is that our experiences do not all blur together; the features of “remembered” events seem to cohere into memories for unique events, even for similar events. Using two measures of representational similarity in fMRI (pattern similarity and repetition suppression), we sought evidence about what enables mnemonic discrimination. In Experiment 2, we found evidence that reactivation of an earlier stimulus while viewing a second helps participants later remember them as distinct episodes. High pattern similarity predicted memory for differences (Figure 5). Furthermore, we found evidence that the hippocampus is involved in reactivation; pattern similarity in the hippocampus was related to pattern similarity in areas of visual cortex in both experiments and, in Experiment 2, hippocampal activity during the second presentation correlated with pattern similarity in visual cortex.

These findings are consistent with previous findings that the HC is important for reactivation (Eldridge et al., 2000; Giovanello, Schnyer, & Verfaellie, 2004; Gordon, Rissman, Kiani, & Wagner, 2013; Ritchey, Wing, LaBar, & Cabeza, 2013; Bosch, Jehee, Fernández, & Doeller, 2014; Staresina, Henson, Kriegeskorte, & Alink, 2012; Wing, Ritchey, & Cabeza, 2015), with the idea that hippocampal reactivation is a mechanism by which features of episodic memories can be bound across time and space (Johnson & Chalfonte, 1994; Wallenstein et al., 1998; Cohen et al., 1999; Davachi & Wagner, 2002; Davachi, 2006; Staresina & Davachi, 2009; Ranganath, 2010), and central to the concept that “reminders” bind events (Hintzman, 2004; 2010). The important role that hippocampally-mediated reactivation plays

in reducing interference and facilitating inferences is also beginning to receive attention (Zeithamova & Preston, 2010; Brown & Stern, 2014; Kuhl et al., 2010; Schlichting et al., 2014). Our findings extend the current understanding in three important ways. First, we demonstrate stimulus-specific reactivation while most previous fMRI work illustrates reactivation at the category level. Second, we provide evidence consistent with a specific type of hippocampal processing – reactivation (i.e., pattern completion or reminding) – for remembering distinct episodic events. Third, the benefit of reactivation in this study extends beyond improved memory for the specific item being reactivated to memory that two similar but not identical items were encountered.

We found much stronger evidence that reactivation helps participants remember pairs as different in Experiment 2 than in Experiment 1. One possibility is that reactivation occurred in Experiment 1, but we were unable to detect it because of the larger perceptual differences between stimuli. Experiment 1 included object exemplars that varied in shape, color, size, etc., while Experiment 2 included scene repeats that varied only in terms of the presence or absence of color. This is consistent with finding that representational *dissimilarity* in LOC (*low* repetition suppression, perhaps due to relatively large perceptual differences) marginally related to memory for differences. Alternatively, reactivation may have been less likely to occur in Experiment 1. Perhaps the difference in stimulus pairs in Experiment 1 and 2 (object exemplars versus nearly identical scenes) or tasks (probability of encountering the object vs. aesthetic judgment) differentially promoted reactivation. However, participants reported spontaneously remembering the first presentation while viewing the second presentation in both experiments. Finally, it is possible that reactivation occurred in Experiment 1 but it did not predict performance. In Experiment 1, many features could distinguish the paired objects whereas in Experiment 2, participants knew that only one discriminating feature – color – varied between repeated stimuli. Therefore, participants in Experiment 2 may have been more likely to reactivate and/or note diagnostic information than those in Experiment 1. If participants in Experiment 1 reactivated non-diagnostic information, any resulting pattern similarity between the 1st and 2nd presentation may not relate to subsequent memory for a difference.

We also found much stronger effects using pattern similarity as opposed to repetition suppression. The differences between these two measures are not entirely clear (see Davis & Poldrack, 2013) but our findings are consistent with previous findings that link pattern similarity to explicit memory (e.g., Ward et al. 2013). They are also consistent with studies linking pattern similarity to reactivation (Gordon, Rissman, Kiani, & Wagner, 2013; Ritchey, Wing, LaBar, & Cabeza, 2013; Bosch, Jehee, Fernández, & Doeller, 2014; Staresina, Henson, Kriegeskorte, & Alink, 2012; Wing, Ritchey, & Cabeza, 2015). In contrast, repetition suppression strongly predicted the true presentation condition of repeats (higher repetition suppression for Identical than Exemplar repeats) in multiple regions in both experiments (Experiment 1: FUS $B=0.60$, $SE=0.15$, $p<0.001$; PHC $B=0.46$, $SE=0.17$, $p<0.01$; all other p 's >0.10 . Experiment 2: LOC $B=0.33$, $SE=0.11$, $p<0.01$; FUS $B=0.79$, $SE=0.19$, $p<0.001$; PHC $B=1.04$, $SE=0.23$, $p<0.001$; ERC $B=0.69$, $SE=0.27$, $p<0.05$; HIP $p>0.10$), suggesting that our experimental design allowed detection of repetition suppression effects. These results are also consistent with repetition suppression indexing the similarity of perceptual rather than reflective representations (Chun & Johnson, 2011).

It should be noted that we are not concluding that reactivation is *required* to encode separable memories. Merely forming a distinct conjunctive representation of each event (presumably comprised of both common and discriminating features) may support mnemonic discrimination. In this case, a cue may later activate each conjunction, and the two representations may be discriminated at test. Indeed, some researchers argue that regions throughout visual cortex, and not just the hippocampus, are capable of binding features and thus, presumably, would support mnemonic discrimination of different feature combinations (Cowell, Bussey, & Saksida, 2010; Shimamura, 2010; Cowell, 2012). However, if this possibility fully explained the lack of subsequent memory effects in Experiment 1, we might expect *distinct* representations to predict memory for difference in Experiment 1. It also should be noted that different regions of the HC may be involved in encoding distinct representations and reactivating previous representations (Marr, 1971; O'Reilly & McClelland, 1994). Our scan parameters were not optimized for distinguishing HC subregions (Yushkevich et al., 2015).

Conclusions

Episodic remembering is the experience of mental representations that seem unique—that is, differentiable from other previous experiences. In two studies directed at clarifying encoding mechanisms that might contribute to later mnemonic discrimination, we found evidence for a reactivation-based mechanism. Thus, our findings support the hypothesis that the hippocampus contributes to encoding unique memories in part through the reactivation of similar memories from the past.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

We thank Su Mei Lee, Kyungmi Kim, and Zarrar Shezhad for insightful comments on the development of the project and manuscript. This research was supported by National Institutes of Health grant number R37AG009253 and the Yale University FAS Imaging Fund.

References

- Bakker A, Kirwan CB, Miller M, Stark CEL. Pattern separation in the human hippocampal CA3 and dentate gyrus. *Science*. 2008; 319(5870):1640–1642. <http://doi.org/10.1126/science.1152882>. [PubMed: 18356518]
- Barnes JM, Underwood BJ. “Fate” of first-list associations in transfer theory. *Journal of Experimental Psychology*. 1959; 58(2):97–105. <http://doi.org/10.1037/h0047507>. [PubMed: 13796886]
- Bates D, Maechler M, Bolker B, Walker S. lme4: Linear mixed-effects models using Eigen and S4. R Package Version. 2013
- Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society Series B*. 1995; 57:289–300.
- Bosch SE, Jehee JFM, Fernández G, Doeller CF. Reinstatement of associative memories in early visual cortex is signaled by the hippocampus. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2014; 34(22):7493–7500. <http://doi.org/10.1523/JNEUROSCI.0805-14.2014>. [PubMed: 24872554]

- Brady TF, Konkle T, Alvarez GA, Oliva A. Visual long-term memory has a massive storage capacity for object details. *Proceedings of the National Academy of Sciences*. 2008; 105(38):14325–14329. <http://doi.org/10.1073/pnas.0803390105>.
- Bransford JD, Johnson MK. Contextual prerequisites for understanding: Some investigations of comprehension and recall. *Journal of Verbal Learning and Verbal Behavior*. 1972; 11(6):717–726. [http://doi.org/10.1016/S0022-5371\(72\)80006-9](http://doi.org/10.1016/S0022-5371(72)80006-9).
- Bransford JD, Johnson MK, Chase WG. Considerations of some problems of comprehension. *Visual Information Processing*. 1973
- Brown TI, Stern CE. Contributions of medial temporal lobe and striatal memory systems to learning and retrieving overlapping spatial memories. *Cerebral Cortex*. 2014; 24(7):1906–1922. <http://doi.org/10.1093/cercor/bht041>. [PubMed: 23448868]
- Chun M, Johnson M. Memory: Enduring Traces of Perceptual and Reflective Attention. *Neuron*. 2011
- Cohen NJ, Ryan J, Hunt C, Romine L, Wszalek T. Hippocampal system and declarative (relational) memory: summarizing the data from functional neuroimaging studies. *Hippocampus*. 1999; 9:83–98. [PubMed: 10088903]
- Cowell RA. Computational models of perirhinal cortex function. *Hippocampus*. 2012; 22(10):1952–1964. <http://doi.org/10.1002/hipo.22064>. [PubMed: 22987674]
- Cowell RA, Bussey TJ, Saksida LM. Components of recognition memory: Dissociable cognitive processes or just differences in representational complexity? *Hippocampus*. 2010; 20(11):1245–1262. <http://doi.org/10.1002/hipo.20865>. [PubMed: 20882548]
- Cox RW. AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research*. 1996; 29:162–173. [PubMed: 8812068]
- Damasio A, Yamada T, Damasio H, Corbett J, McKee J. Central achromatopsia: Behavioral, anatomic, and physiologic aspects. *Neurology*. 1980; 30(10):1064–1071. [PubMed: 6968419]
- Davachi L. Item, context and relational episodic encoding in humans. *Current Opinion in Neurobiology*. 2006; 16(6):693–700. <http://doi.org/10.1016/j.conb.2006.10.012>. [PubMed: 17097284]
- Davachi L, Wagner AD. Hippocampal contributions to episodic encoding: insights from relational and item-based learning. *Journal of Neurophysiology*. 2002; 88(2):982–990. [PubMed: 12163547]
- Davis, T.; Poldrack, RA. Measuring neural representations with fMRI: practices and pitfalls.. *Annals of the New York Academy of Sciences*. 2013. n/a–n/a. <http://doi.org/10.1111/nyas.12156>
- Eichenbaum H, Yonelinas AR, Ranganath C. The medial temporal lobe and recognition memory. *Annual review of neuroscience*. 2007; 30(1):123–152.
- Eldridge LL, Knowlton BJ, Furmanski CS, Bookheimer SY, Engel SA. Remembering episodes: a selective role for the hippocampus during retrieval. *Nature Neuroscience*. 2000; 3(11):1149–1152. [PubMed: 11036273]
- Epstein RA, Parker WE, Feller AM. Two kinds of fMRI repetition suppression? Evidence for dissociable neural mechanisms. *Journal of Neurophysiology*. 2008; 99(6):2877–2886. [PubMed: 18400954]
- Fischl B. FreeSurfer. *Neuroimage*. 2012; 62:774–781. [PubMed: 22248573]
- Giovanello KS, Schnyer DM, Verfaellie M. A critical role for the anterior hippocampus in relational memory: evidence from an fMRI study comparing associative and item recognition. *Hippocampus*. 2004; 14(1):5–8. [PubMed: 15058477]
- Gordon, AM.; Rissman, J.; Kiani, R.; Wagner, AD. Cortical Reinstatement Mediates the Relationship Between Content-Specific Encoding Activity and Subsequent Recollection Decisions.. *Cerebral Cortex*. 2013. <http://doi.org/10.1093/cercor/bht194>
- Grill-Spector K, Malach R. The human visual cortex. *Annual Review Neuroscience*. 2004; 27:649–677.
- Henkel LA. Erroneous memories arising from repeated attempts to remember. *Journal of Memory and Language*. 2004; 50:26–46.
- Hintzman DL. Judgment of frequency versus recognition confidence: Repetition and recursive reminding. *Memory & Cognition*. 2004; 32(2):336–350. [PubMed: 15190724]

- Hintzman DL. How does repetition affect memory? Evidence from judgments of recency. *Memory & Cognition*. 2010; 38(1):102–115. [PubMed: 19966243]
- Johnson, MK.; Chalfonte, BL. Binding complex memories: The role of reactivation and the hippocampus. The MIT Press; 1994.
- Johnson MK, Hashtroudi S, Lindsay DS. Source Monitoring. *Psychological Bulletin*. 1993; 114(1):3–28. [PubMed: 8346328]
- Johnson, MK.; Hirst, W. Theories of Memory. Erlbaum; East Sussex, England: 1993.
- Kuhl BA, Chun MM. Successful remembering elicits event-specific activity patterns in lateral parietal cortex. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2014; 34(23):8051–8060. [PubMed: 24899726]
- Kuhl BA, Bainbridge WA, Chun MM. Neural reactivation reveals mechanisms for updating memory. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2012; 32(10):3453–3461. <http://doi.org/10.1523/JNEUROSCI.5846-11.2012>. [PubMed: 22399768]
- Kuhl BA, Shah AT, DuBrow S, Wagner AD. Resistance to forgetting associated with hippocampus-mediated reactivation during new learning. *Nature Neuroscience*. 2010; 13(4):501–506. <http://doi.org/10.1038/nn.2498>. [PubMed: 20190745]
- Lacy JW, Yassa MA, Stark SM, Muftuler LT, Stark CEL. Distinct pattern separation related transfer functions in human CA3/dentate and CA1 revealed using high-resolution fMRI and variable mnemonic similarity. *Learning & Memory (Cold Spring Harbor, NY)*. 2011; 18(1):15–18. <http://doi.org/10.1101/lm.197111>.
- LaRocque KF, Smith ME, Carr VA, Witthoft N, Grill-Spector K, Wagner AD. Global similarity and pattern separation in the human medial temporal lobe predict subsequent memory. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2013; 33(13):5466–5474. <http://doi.org/10.1523/JNEUROSCI.4293-12.2013>. [PubMed: 23536062]
- Lu Y, Wang C, Chen C, Xue G. Spatiotemporal neural pattern similarity supports episodic memory. *Current Biology : CB*. 2015; 25(6):780–785. <http://doi.org/10.1016/j.cub.2015.01.055>. [PubMed: 25728695]
- Malach R, Reppas JB, Benson RR, Kwong KK, Jiang H, Kennedy WA, et al. Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proceedings of the National Academy of Sciences of the United States of America*. 1995; 92(18):8135–8139. [PubMed: 7667258]
- Manelis A, Paynter CA, Wheeler ME, Reder LM. Repetition related changes in activation and functional connectivity in hippocampus predict subsequent memory. *Hippocampus*. 2013
- Manelis A, Wheeler ME, Paynter CA, Storey L, Reder LM. Opposing patterns of neural priming in same-exemplar vs. different-exemplar repetition predict subsequent memory. *NeuroImage*. 2011; 55(2):763–772. <http://doi.org/10.1016/j.neuroimage.2010.12.034>. [PubMed: 21168518]
- Marr D. Simple memory: a theory for archicortex. *Philosophical Transactions of the Royal Society of London, B, Biological Sciences*. 1971; 262(841):23–81. [PubMed: 4399412]
- Norman KA. How hippocampus and cortex contribute to recognition memory: Revisiting the complementary learning systems model. *Hippocampus*. 2010; 20(11):1217–1227. <http://doi.org/10.1002/hipo.20855>. [PubMed: 20857486]
- Norman KA, O'Reilly RC. Modeling hippocampal and neocortical contributions to recognition memory: a complementary-learning-systems approach. *Psychological Review*. 2003; 110(4):611–646. <http://doi.org/10.1037/0033-295X.110.4.611>. [PubMed: 14599236]
- Norman KA, Polyn SM, Detre GJ, Haxby JV. Beyond mind-reading: multi-voxel pattern analysis of fMRI data. *Trends in Cognitive Sciences*. 2006; 10(9):424–430. [PubMed: 16899397]
- O'Reilly RC, McClelland JL. Hippocampal conjunctive encoding, storage, and recall: avoiding a trade-off. *Hippocampus*. 1994; 4(6):661–682. [PubMed: 7704110]
- Pearlman AL, Birch J, Meadows JC. Cerebral color blindness: an acquired defect in hue discrimination. 1979
- Postman L, Parker F. Maintenance of first-list associations during transfer. *The American Journal of Psychology*. 1970; 83(2):171–188.
- R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing; Vienna, Austria: 2015. URL <http://www.R-project.org/>

- Ranganath C. A unified framework for the functional organization of the medial temporal lobes and the phenomenology of episodic memory. *Hippocampus*. 2010; 20(11):1263–1290. <http://doi.org/10.1002/hipo.20852>. [PubMed: 20928833]
- Rasch B, Born J. Maintaining memories by reactivation. *Current Opinion in Neurobiology*. 2007; 17(6):698–703. <http://doi.org/10.1016/j.conb.2007.11.007>. [PubMed: 18222688]
- Ritchey M, Wing EA, LaBar KS, Cabeza R. Neural similarity between encoding and retrieval is related to memory via hippocampal interactions. *Cerebral Cortex*. 2013; 23(12):2818–2828. <http://doi.org/10.1093/cercor/bhs258>. [PubMed: 22967731]
- Roediger HL, Karpicke JD. Test-enhanced learning: taking memory tests improves long-term retention. *Psychological Science : a Journal of the American Psychological Society / APS*. 2006; 17(3):249–255. <http://doi.org/10.1111/j.1467-9280.2006.01693.x>.
- Schlichting ML, Zeithamova D, Preston AR. CA1 subfield contributions to memory integration and inference. *Hippocampus*. 2014; 24(10):1248–1260. <http://doi.org/10.1002/hipo.22310>. [PubMed: 24888442]
- Shimamura AP. Hierarchical relational binding in the medial temporal lobe: the strong get stronger. *Hippocampus*. 2010; 20(11):1206–1216. <http://doi.org/10.1002/hipo.20856>. [PubMed: 20824723]
- Staresina BP, Davachi L. Mind the gap: binding experiences across space and time in the human hippocampus. *Neuron*. 2009; 63(2):267–276. <http://doi.org/10.1016/j.neuron.2009.06.024>. [PubMed: 19640484]
- Staresina BP, Henson RNA, Kriegeskorte N, Alink A. Episodic reinstatement in the medial temporal lobe. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2012; 32(50):18150–18156. <http://doi.org/10.1523/JNEUROSCI.4156-12.2012>. [PubMed: 23238729]
- Tulving, E. Episodic and semantic memory.. In: Tulving, E.; Donaldson, W., editors. *Organization of Memory*. Academic Press; New York: 1972.
- Turk-Browne NB, Yi D-J, Leber AB, Chun MM. Visual Quality Determines the Direction of Neural Repetition Effects. *Cerebral Cortex*. 2006; 17(2):425–433. <http://doi.org/10.1093/cercor/bhj159>. [PubMed: 16565294]
- Underwood BJ. Attributes of memory. *Psychological Review*. 1969; 76(6):559–573.
- Wahlheim CN, Jacoby LL. Remembering change: the critical role of recursive reminders in proactive effects of memory. *Memory & Cognition*. 2013; 41(1):1–15. <http://doi.org/10.3758/s13421-012-0246-9>. [PubMed: 22918874]
- Wallenstein GV, Eichenbaum H, Hasselmo ME. The hippocampus as an associator of discontinuous events. *Trends in Neurosciences*. 1998; 21(8):317–323. [PubMed: 9720595]
- Ward EJ, Chun MM, Kuhl BA. Repetition suppression and multi-voxel pattern similarity differentially track implicit and explicit visual memory. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2013; 33(37):14749–14757. <http://doi.org/10.1523/JNEUROSCI.4889-12.2013>. [PubMed: 24027275]
- Wing EA, Ritchey M, Cabeza R. Reinstatement of individual past events revealed by the similarity of distributed activation patterns during encoding and retrieval. *Journal of Cognitive Neuroscience*. 2015; 27(4):679–691. http://doi.org/10.1162/jocn_a_00740. [PubMed: 25313659]
- Xue G, Dong Q, Chen C, Lu Z, Mumford JA, Poldrack RA. Greater neural pattern similarity across repetitions is associated with better memory. *Science*. 2010; 330(6000):97–101. <http://doi.org/10.1126/science.1193125>. [PubMed: 20829453]
- Xue G, Dong Q, Chen C, Lu Z-L, Mumford JA, Poldrack RA. Complementary role of frontoparietal activity and cortical pattern similarity in successful episodic memory encoding. *Cerebral Cortex*. 2013; 23(7):1562–1571. [PubMed: 22645250]
- Yassa MA, Stark CEL. Pattern separation in the hippocampus. *Trends in Neurosciences*. 2011; 34(10):515–525. [PubMed: 21788086]
- Yushkevich PA, Amaral RSC, Augustinack JC, Bender AR, Bernstein JD, Boccardi M, et al. Quantitative comparison of 21 protocols for labeling hippocampal subfields and parahippocampal subregions in in vivo MRI: towards a harmonized segmentation protocol. *NeuroImage*. 2015; 111:526–541. <http://doi.org/10.1016/j.neuroimage.2015.01.004>. [PubMed: 25596463]
- Zeidman P, Mullally SL, Maguire EA. Constructing, perceiving, and maintaining scenes: Hippocampal activity and connectivity. *Cerebral Cortex*. 2015; 25:3836–3855. [PubMed: 25405941]

- Zeithamova D, Preston AR. Flexible memories: differential roles for medial temporal lobe and prefrontal cortex in cross-episode binding. *The Journal of Neuroscience : the Official Journal of the Society for Neuroscience*. 2010; 30(44):14676–14684. <http://doi.org/10.1523/JNEUROSCI.3250-10.2010>. [PubMed: 21048124]
- Zeki S. A century of cerebral achromatopsia. *Brain*. 1990; 113(6):1721–1777. [PubMed: 2276043]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Figure 1.

Scanned encoding task and example stimuli for each experiment (Experiment 1 on the left, Experiment 2 on the right). There were three presentation conditions: single presentation (bed; coral reef), identical repeat (broccoli; empire state building), or exemplar repeat (baseball glove; baseball park). The inter-stimulus-interval in Experiment 1 was 2, 4, or 6 seconds and in Experiment 2 was 5.5, 7.0, or 8.5 seconds.

Figure 2.

Anatomical ROIs of representative participants within each experiment. In both cases the hippocampus (HC), entorhinal cortex (ERC), parahippocampal cortex (PHC), lateral occipital cortex (LOC), and fusiform cortex (FUS) were defined anatomically using FreeSurfer's automated cortical segmentation. In Experiment 1, the LOC was of particular interest as an area known to contain object information and in Experiment 2, the FUS was of particular interest because it is known to be color sensitive. Mean voxel counts for Experiment 1 are: LOC = $4,232 \pm 730$, FUS = 3370 ± 454 , PHC = 754 ± 81 , ERC = 490 ± 117 , HC = 1128 ± 132 . Mean voxel counts for Experiment 2 are: LOC = 3629 ± 446 , FUS = 2792 ± 388 , PHC = 640 ± 74 , ERC = 421 ± 49 , HC = 1066 ± 81 .

Figure 3. The rate of each Response type (e.g., “Never”) for each Presentation condition (e.g., Lure) for Experiment 1 (top) and Experiment 2 (bottom).

Figure 4.
Predicted results for reactivation and distinctive encoding hypotheses.

Figure 5.

Fitted logistic regressions predicting participants' Response (correct "Twice-Different" vs. incorrect "Twice-Identical") from pattern similarity for each experiment. Error bands show the 95% confidence interval for the predicted function. Confidence intervals were drawn by defining an upper and lower bound on the estimated beta and plotting the associated logistic curve. For a given estimated beta, β (e.g., for the LOC pattern similarity predictor), the upper bound beta, β_U was defined as: $\beta + 1.96 \cdot SE_b$ where SE_b is the estimated standard error of β . The lower bound beta, β_L was defined as $\beta - 1.96 \cdot SE_b$. The logistic curves defined by β_U and β_L are plotted in dotted red and blue lines, respectively. In Experiment 1, higher pattern similarity in FUS marginally predicted correct responses and in Experiment 2, higher pattern similarity in all regions predicted correct responses (see text).

Figure 6.

Fitted logistic regressions predicting participants' Response (correct "Twice-Different" vs. incorrect "Twice-Identical") from repetition suppression for each experiment. Error bands show the 95% confidence interval for the predicted function. Confidence intervals were drawn by defining an upper and lower bound on the estimated beta and plotting the associated logistic curve. For a given estimated beta, β (e.g., for the LOC pattern similarity predictor), the upper bound beta, β_U was defined as: $\beta + 1.96 \cdot SE_b$ where SE_b is the estimated standard error of β . The lower bound beta, β_L was defined as $\beta - 1.96 \cdot SE_b$. The logistic curves defined by β_U and β_L are plotted in dotted red and blue lines, respectively. In Experiment 1, lower repetition suppression in LOC marginally predicted correct responses and in Experiment 2, higher repetition suppression in HC marginally predicted correct responses (see text).