Supplemental Information

Similarity Breeds Proximity: Pattern Similarity Within and Across Contexts is Related to Later Mnemonic Judgments of Temporal Proximity

Youssef Ezzyat and Lila Davachi

Supplemental Data

Overall Measures of Pattern Similarity

The first analysis was designed to ask whether pattern similarity (PS) across trials is related to *objective* temporal distance between trials (i.e. trials that are closer together should show greater PS than trials that are further apart). We reasoned that if PS as a dependent measure is related to temporal/context representations, we should indeed see that similarity is greater for trials that are closer together in time. We first conducted this analysis in a mask of task-active voxels distributed across the whole brain (*Whole-Brain Mask Definition*, see Supplemental Experimental Procedures) and found that PS was significantly greater for consecutive trials compared to non-consecutive trials across a range of mask sizes (500-10,000 voxels; all $p < .002$). We also observed significantly greater PS for consecutive trials compared to non-consecutive trials in all of our individual regions of interest, including left hippocampus ($p < .001$) and left LO ($p < .03$). Having confirmed that PS was related to objective temporal distance, our remaining analyses examined how PS is related to subjective mnemonic judgments of temporal distance and shifts in context for pairs of trials matched for actual temporal distance.

Overall Measures of Pattern Similarity in Category-Responsive ROIs

We examined the relationship between pattern similarity (PS) and objective temporal distance in the following functionally-defined stimulus category-selective regions of interest (ROIs): parahippocampal place area (PPA), fusiform place area (FFA) and retrosplenial cortex (RSC). This analysis compared PS for consecutive pairs of items to PS for non-consecutive pairs of items (see also *Overall Measures of Pattern Similarity* in the main text) and revealed that all ROIs in both hemispheres showed enhanced PS for consecutive trials relative to non-consecutive trials (all $p < .04$) with the exception of left FFA [$t(10) = 1.70$, $p > .12$].

Logistic Regression Analysis

In order to further examine the specificity of PS in left hippocampus and temporal distance judgments, we conducted a complementary logistic regression analysis in which we included the mean univariate BOLD activation in left hippocampus for each of the encoding trials, in addition to PS between trials, in a model to predict *close*/*far* responses. The resulting beta coefficients for each of the three predictors were then tested for significance across the group (one-sample *t*-test against zero) and were also tested against each other to determine any relative differences in their contributions to temporal memory. In left hippocampus, neither

mean activation for the first trial of a pair [beta = -.006 ± .006; $p > .31$] nor the second trial of a pair [beta = -.003 ± .006; $p > .65$] were significant predictors of *close*/*far* response. In contrast, PS across trials was a significant predictor of memory response [beta = .344 ± .156; $t(17) = 2.26$, $p < .04$], consistent with the results from our first analysis examining the relationship between mean PS and memory response. In addition, PS beta estimates were significantly higher than both first trial [$t(17) = 2.35$, $p < .04$] and second trial [$t(17) = 2.24$, $p < .04$] mean activation beta estimates, indicating that PS was a significantly better predictor of *close*/*far* responses than mean activation on either trial. Taken together, the logistic regression analyses show that when overall BOLD activation and PS are analyzed within the same model, BOLD activation is not a significant predictor of later temporal memory and PS is significantly more predictive of temporal memory than the univariate activation on either encoding trial.

We also conducted logistic regression analyses to predict memory responses separately within the *boundary* and *same context* conditions. Mirroring our findings from the PS analysis above, a logistic regression analysis limited to *boundary* trials showed that PS was a significant predictor of memory response [beta = .838 ± .354; $t(16) = 2.09$, $p < .03$]. This effect was not observed within the *same context* condition ($p > .75$); however the difference between the *context boundary* and *same context* PS beta estimates was not significant ($p > .14$).

We conducted logistic regression analyses in left LO in order to determine the contributions of PS and mean ROI BOLD activation on later memory responses. Consistent with our results using mean PS, the level of PS between trials was found to be a significant predictor of memory response only for *same context* pairs [beta = .682 ± .204; $t(11) = 3.42$, $p < .006$]. In contrast, mean activation on the first trial [beta = .010 ± .011; $p > .36$] and second trial [beta = -.038 ± .022; $p > .10$] were not significant predictors of memory response. Furthermore, direct comparisons of beta estimates for PS and mean activation showed PS estimates to be significantly greater than mean activity estimates on both the first [$t(11) = 3.49$, $p < .006$] and second trials [$t(11) = 3.50$, $p < .005$], indicating that PS in LO in the *same context* condition was significantly better at predicting temporal memory responses than mean activation on either trial. In contrast to the *same context* results, none of the three variables was found to be a significant predictor of memory response on *boundary* trials, nor when collapsing across *boundary*/*same context* (all $p > .10$).

Pattern Similarity Searchlight

As described in the main text, we conducted a searchlight analysis to examine PS effects in local regions across the whole brain. We compared PS for *close* and *far* pairs

collapsed across *context boundary* and *same context* conditions, as well as within each condition separately, finding no significant regions at a mapwise corrected threshold of $p < .05$. To explore whether subthreshold effects might nonetheless be present, we conducted the same comparisons at a more liberal threshold (voxel-wise $p < .005$ and ten voxel cluster minimum). At this relaxed threshold we still did not observe any regions showing enhanced PS for close pairs relative to far pairs collapsed across context condition. Within the *context boundary* condition, only one region in right dorsolateral prefrontal cortex (PFC) showed greater similarity for *close* pairs compared to *far* pairs. In the *same context* condition one region in the right amygdala showed the reverse effect—greater similarity for *far* pairs compared to *close* pairs.

Repetition Suppression

We computed trial-by-trial within-participant correlations between RS and PS. The goal of this analysis was to determine whether RS on individual trial pairs was related to PS on the same trial pairs, and to see whether this relationship differed across context and memory conditions in a way that could explain our PS results. This analysis showed that PS and RS were not significantly correlated and that the PS-RS correlations did not significantly differ across context or memory conditions in either hippocampus or LO. Our final analysis examined whether RS itself is related to temporal memory, and also found no significant main effects or interactions in either region. We first conducted separate one-sample *t*-tests within each condition in both regions to test whether *any* of the RS-PS correlations significantly differed from zero. No correlations were significantly greater than zero (all $p > .1$). We then conducted context condition X memory ANOVAs in both left hippocampus and left LO to determine whether the RS-PS correlation differed by experimental condition in either region. This analysis showed no main effects of context type or temporal memory (all p's $> .28$) and no interaction between context type and memory in left hippocampus ($p > .18$), confirming that the RS-PS correlation was equivalent across all conditions in hippocampus. In left LO, the interaction was marginal [$F(1,11) = 3.37$, $p < .1$] and follow-up comparisons revealed no significant differences (all p's $> .12$). Critically, a region X context type X memory ANOVA did not reveal any interactions by region (all $p > .11$), suggesting that the level of correlation between RS and PS in both regions was similar across all conditions. Taken together, these data show that there were no significant correlations between RS and PS in any condition, and that the pattern of these non-significant correlations was not significantly different across regions.

The previous analyses indicate that equivalent levels of RS were observed across left hippocampus and left LO and also show that RS was not significantly related to PS in either

region. Our final analysis explored whether RS is directly related to temporal memory by determining whether mean RS differed according to *context boundary*/*same context* and *close*/*far* memory. We extracted beta estimates for S1 and S2 trials separately for the two context conditions and the two temporal memory conditions. We then took the difference in S1 and S2 (i.e. computed RS) for each condition and analyzed the resulting differences with a context type X memory response ANOVA. There were no significant main effects or interactions in either hippocampus (all $p > .28$) or LO (all $p > .23$).

Supplemental Figures

Figure S1, Related to Figure 2. Source Memory as a Function of Temporal Memory
Sorting source memory accuracy (e.g. memory for the scene-item association) according to temporal memory response (*close*/*far*) showed a marginal difference in source memory for same context trials labeled *close* compared to *far*.

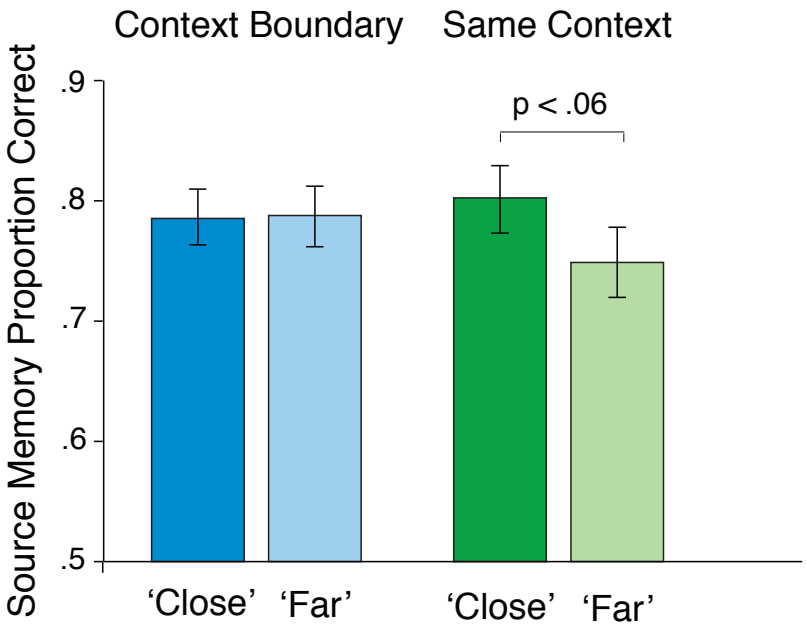
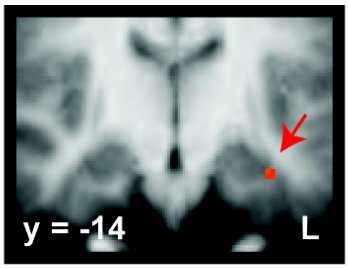


Figure S2, Related to Figure 3A. Univariate Source Memory Analysis

A voxel-wise contrast of source correct > source incorrect (misses) revealed a cluster in left hippocampus (-36, -14, -18) in which encoding activation was associated with high-confidence correct source memory (voxel-wise $p < .005$, cluster size minimum = 5 voxels).



Left Hippocampus

Figure S3, Related to Figure 3B and D. Pattern Similarity in PPA, FFA and RSC

Unlike left hippocampus and left LO, pattern similarity in other brain areas responsive to the experimental stimuli, such as parahippocampal place area (PPA), fusiform face area (FFA) and retrosplenial cortex (RSC) did not differ based on the context boundary manipulation nor by mnemonic temporal distance response. Left panel: PPA, FFA and RSC regions of interest from representative participants. Right panel: mean pattern similarity computed within each region. Error bars denote standard error of the mean.

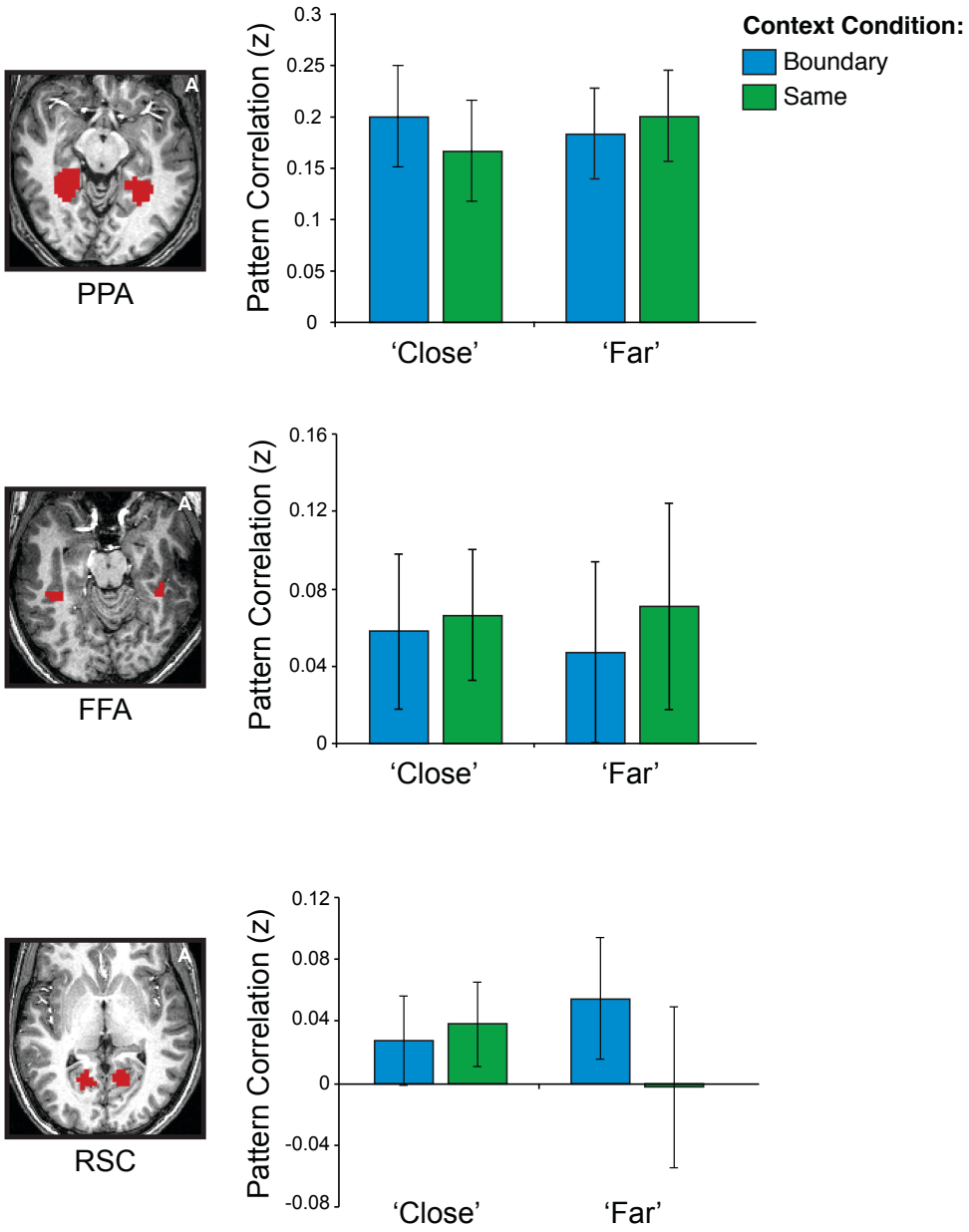
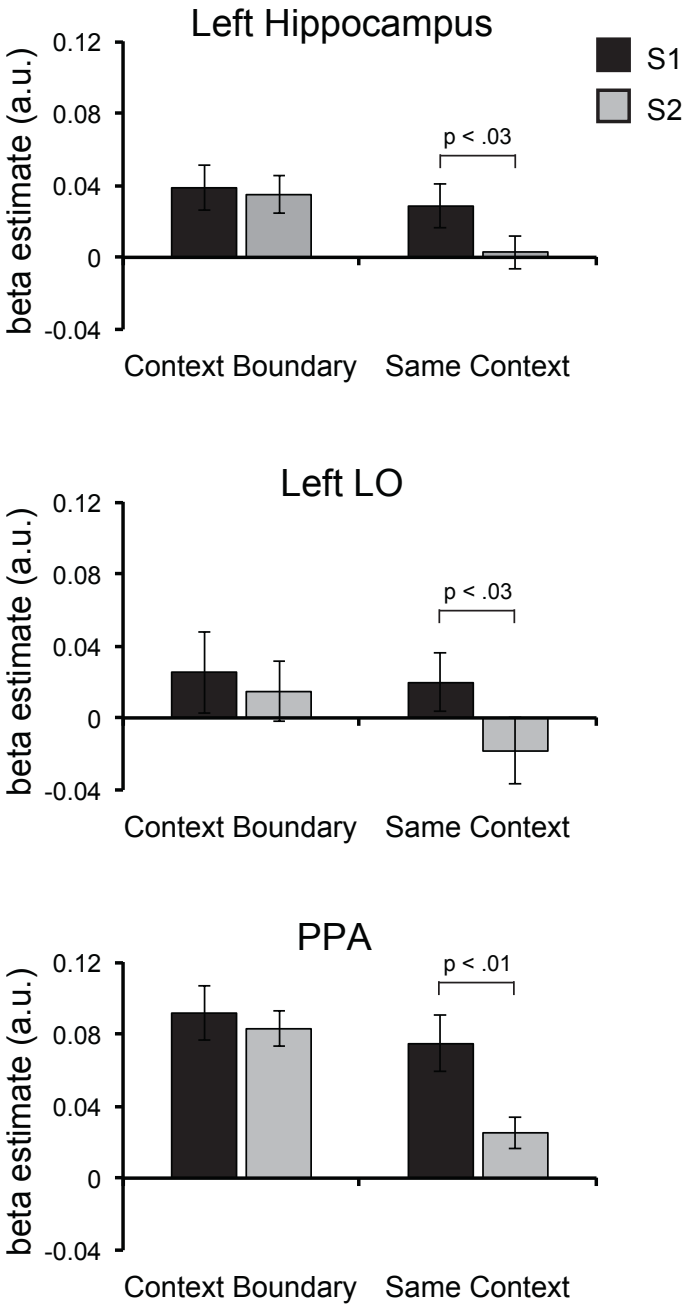


Figure S4, Related to Figure 3. Repetition Suppression Effects

Marginal repetition suppression was observed in left hippocampus and left LO, with stronger effects in both regions in the *same context* condition. Significant repetition suppression was observed in PPA (averaged left/right). Top panel: hippocampus; middle panel: LO; bottom panel: PPA.



Supplemental Tables

Table S1, Related to Figure 3A. Regions emerging from High-Confidence Source Hits > Misses. Minus sign (-) denotes deactivation.

Univariate Source Memory Contrast	MNI Coordinates
Frontal, Parietal and Occipital Lobes (p < .001)	
Right angular gyrus (-)	(57, -56, 41)
Right inferior frontal gyrus (-)	(39, 54, 1)
Right middle occipital gyrus	(40, -75, 18)
Right lateral orbitofrontal gyrus (-)	(28, 23, -8)
Right middle frontal gyrus (-)	(23, 61, 11)
Right anterior cingulate gyrus (-)	(10, 37, 20)
Right superior frontal gyrus (-)	(5, 66, 16)
Left superior frontal gyrus	(-12, 19, 62)
Left gyrus rectus (-)	(-15, 32, -15)
Left precuneus	(-22, -73, 38)
Left middle frontal gyrus	(-26, 13, 58)
Left superior parietal gyrus	(-26, -75, 42)
Left cerebellum	(-30, -48, -18)
Left middle orbitofrontal gyrus	(-33, 33, -6)
Left angular gyrus	(-44, -70, 24)
Left inferior frontal gyrus	(-46, 36, 8)
Left middle frontal gyrus	(-50, 24, 26)
Temporal Lobes (p < .005)	
Right middle temporal gyrus (-)	(67, -22, -18)
Right middle temporal gyrus (-)	(56, -5, -35)
Right inferior temporal gyrus (-)	(52, -21, -37)
Right fusiform gyrus	(40, -42, -14)
Right fusiform gyrus	(36, -38, -24)
Right fusiform gyrus	(28, -47, -10)
Right parahippocampal gyrus	(23, -35, -16)
Left hippocampus	(-36, -14, -18)
Left fusiform gyrus	(-30, -34, -21)
Left parahippocampal gyrus	(-31, -41, -8)
Left fusiform gyrus	(-30, -49, -17)

Table S2, Related to Figure 4. Regions emerging from whole-brain pattern similarity searchlight analysis.

Pattern Similarity Searchlight Contrast	MNI Coordinates
Context Boundary > Same Context	
Right anterior cingulate	(5, 19, 49)
Right intraparietal sulcus	(28, -72, 36)
Left thalamus	(-14, -7, 6)
Left cerebellum	(-16, -47, 23)
Left striatum	(-18, 14, 19)
Left inferior frontal gyrus	(-30, 27, 10)
Left insula	(-38, 15, 2)
Left anterior inferior frontal gyrus	(-41, 34, -1)
Left motor/somatosensory	(-46, -14, 52)
Same Context > Context Boundary	
Right temporo-parietal junction	(46, -38, 2)
Right inferior occipital cortex	(42, -68, -21)
Right dorsal anterior temporal lobe	(36, 14, 22)
Right posterior parahippocampal gyrus	(29, -38, 2)
Right occipital cortex	(28, -83, -5)
Right inferior occipital cortex	(23, -82, 22)
Right cerebellum	(17, -59, -44)
Right medial PFC	(17, 42, 24)
Left motor cortex	(-7, -9, 79)
Left dorsomedial PFC/ACC	(-14, 31, 29)

Supplemental Experimental Procedures

Whole-Brain Mask Definition

We defined a distributed ROI of task-active voxels across the whole brain, in order to assess broad-scale levels of pattern similarity (PS, analysis described below). To define the whole-brain ROI, we used a GLM to model all encoding trials as a single condition. Each trial was modeled as a boxcar spanning the 4-second stimulus presentation duration, convolved with a canonical hemodynamic response function. We then isolated the 5000 most active voxels in a contrast of Task > Baseline; these voxels were used as the input for whole-brain pattern similarity analyses. To conduct the analysis, we computed mean estimates of PS for pairs of encoding trials from the first and last positions of each quartet (i.e. the trials of interest for all remaining analyses) and compared them to mean estimates of PS for pairs of trials from the second and third positions of each quartet. These mean PS estimates were then compared using paired *t*-tests across a range of mask sizes (500-10,000 voxels).

Logistic Regression Analyses

In addition to examining how mean PS at encoding was related to later temporal distance judgments, we also conducted a complementary logistic regression analysis that included both PS and overall activation in our regions of interest as predictors of temporal distance judgments. This analysis allowed us to directly compare the relative contributions of PS and overall BOLD activation in predicting temporal memory responses. For each region of interest, for each participant, we ran a model in which binary memory responses (*close*/*far*) were predicted based on mean ROI activation for the first trial of a pair; mean ROI activation for the second trial of a pair; and pattern similarity between the two trials in the pair (LaRocque et al., 2013; Ritchey et al., 2012). The beta estimates were then tested with one-sample *t*-tests to determine whether they differed significantly from zero across the group. The beta estimates for the mean activation predictors were then compared (using paired *t*-tests) to the beta estimates for PS in order to determine whether mean activation and PS are differentially predictive of temporal memory. Separate logistic regression models were run collapsing across context condition (*boundary*/*same context*) as well as within each context condition individually. One participant with beta estimates greater than 2.5 standard deviations from the mean in one condition was excluded from statistical analyses of the hippocampal data; one such participant was also excluded from statistical analyses of the data in LO.

Pattern Similarity Searchlight Permutation Procedure

Because the searchlight analysis was repeated at each voxel across the whole brain, we used a permutation test to set a cluster size threshold that would result in a map-wise false positive rate of $p < .05$. To do this, we extracted the similarity values for all pairs of *context boundary* and *same context* pairs, and then randomly assigned each pair to either the *close* or *far* bin within each condition. We then computed mean pattern similarity at each voxel for each participant, and then computed paired *t*-tests on these values across the group at each voxel. We applied a threshold of $p < .005$ to this map to generate a set of clusters. The size of the largest cluster in this map was recorded; the entire randomization procedure was then repeated 1000 times in order to generate a distribution of cluster sizes. This distribution was used to select a cluster size corresponding to a corrected $p < .05$ mapwise false positive rate.

Supplemental References

LaRocque, K.F., Smith, M.E., Carr, V.A., Witthoft, N., Grill-Spector, K., and Wagner, A.D. (2013). Global similarity and pattern separation in the human medial temporal lobe predict subsequent memory. The Journal of Neuroscience *33*, 5466–5474.

Ritchey, M., Wing, E.A., Labar, K.S., and Cabeza, R. (2012). Neural Similarity Between Encoding and Retrieval is Related to Memory Via Hippocampal Interactions. Cerebral Cortex *doi:10.109*.