

Object and spatial mnemonic interference differentially engage lateral and medial entorhinal cortex in humans

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Supporting Information (SI) Appendix

Figures S1-S10; Table S1

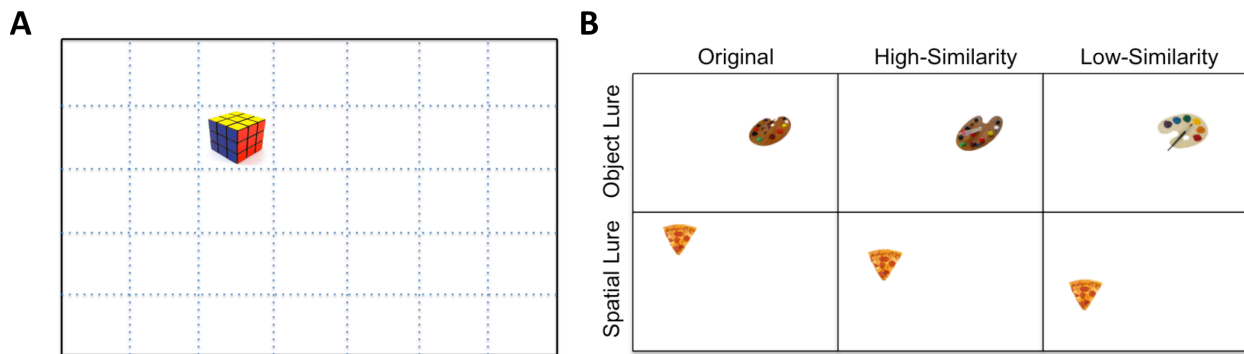


Fig S1. Task design and stimuli. (A) A sample display showing the invisible grid illustrating the possible positions where objects can be displayed on the screen (corner locations were avoided); (B) Sample stimuli showing how object and spatial lures were constructed. High and low similarity object lures were based on prior ratings of these objects' discriminability using performance from an orthogonal sample. High and low similarity spatial lures were based on spatial displacement of 1 (high similarity) or 2 (low similarity) grid locations.

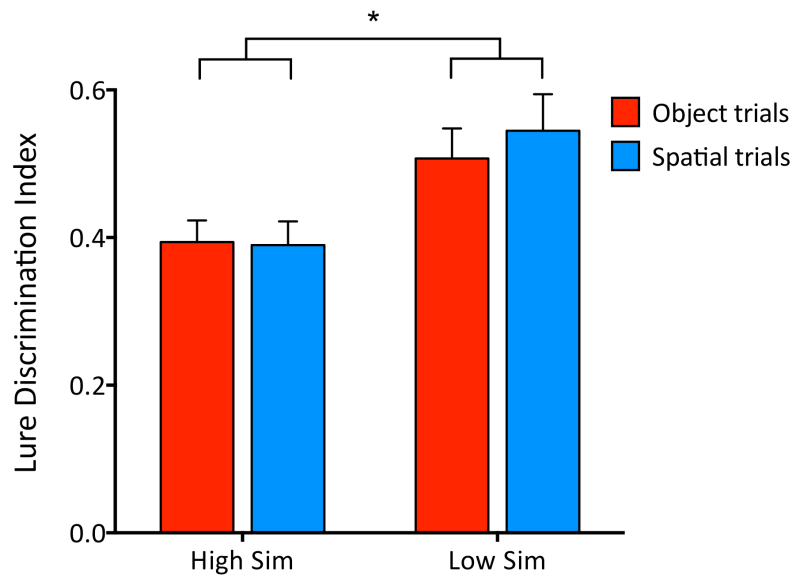


Fig S2. Out-of-scanner behavioral data. A comparison of performance on high and low similarity object and spatial lure trials. The Y-axis is Lure discrimination Index (LDI) which is calculated as $p(\text{"Object Change"}|\text{Object Lure}) - p(\text{"Object Change"}|\text{Novel Foil})$ for object lures and $p(\text{"Spatial Change"}|\text{Spatial Lure}) - p(\text{"Spatial Change"}|\text{Novel Foil})$. These indices correct for participant response bias. There is a main effect of similarity with high similarity items (both object and spatial) being more difficult to discriminate than low similarity items. There is no main effect of trial type (object vs. spatial) and no interaction between trial type and similarity. This pattern of results is similar to the results of the in-scanner behavioral task (Fig 1), although performance in general was better outside the scanner.

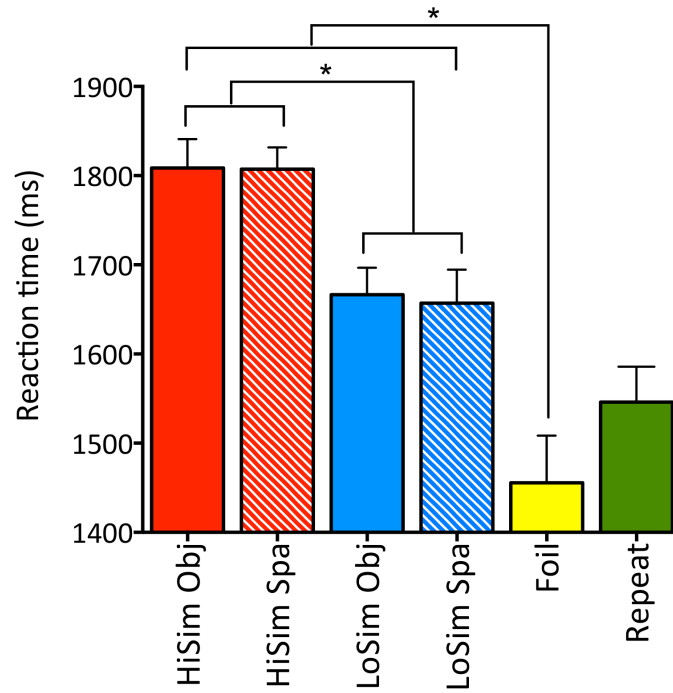


Fig S3. Reaction time data. On average reaction times on lures trials were longer than on foils and repetitions. There was a significant main effect of lure similarity, but no main effect of information domain (object vs. spatial) and no significant interaction. Only correct trials were included here.

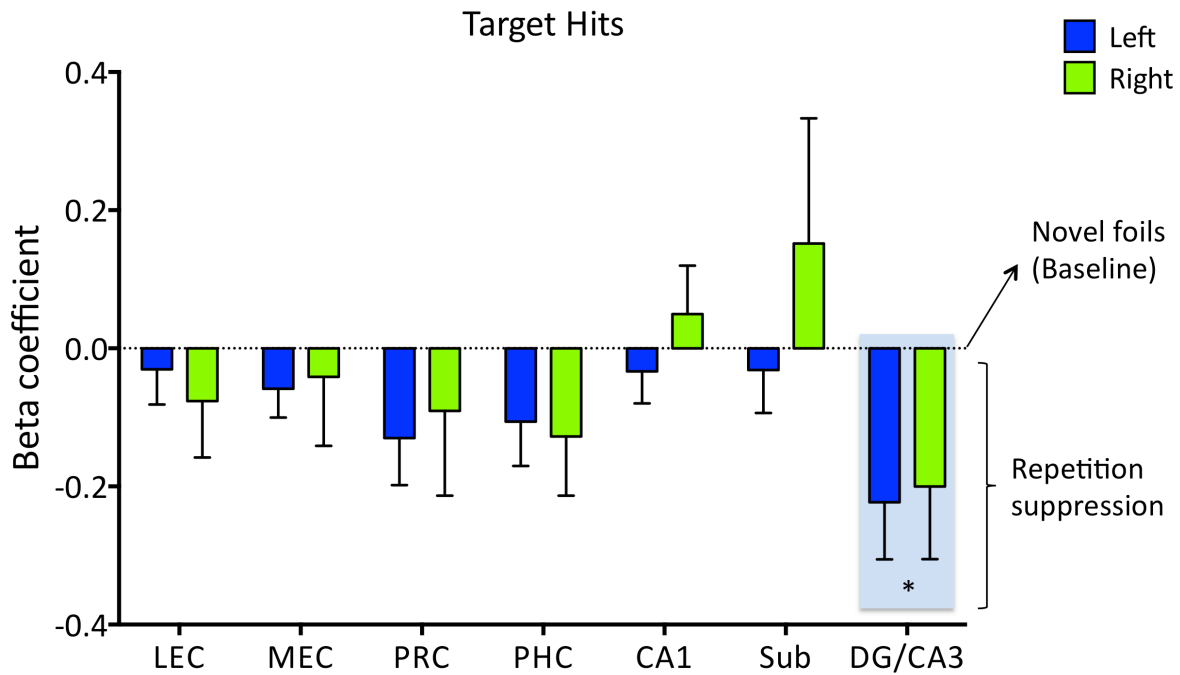


Fig S4. Medial temporal lobe subregion and hippocampal subfield responses during target hits. Correct rejections of novel foils were used as baseline trials. Although most regions (except right CA1 and subiculum) demonstrate below zero responses (i.e. repetition suppression or fMRI adaptation), this effect is most pronounced in the DG/CA3, which is significantly different from all other regions. Abbreviations: LEC: lateral entorhinal cortex, MEC: medial entorhinal cortex, PRC: perirhinal cortex, PHC: parahippocampal cortex, Sub: subiculum, DG: dentate gyrus.

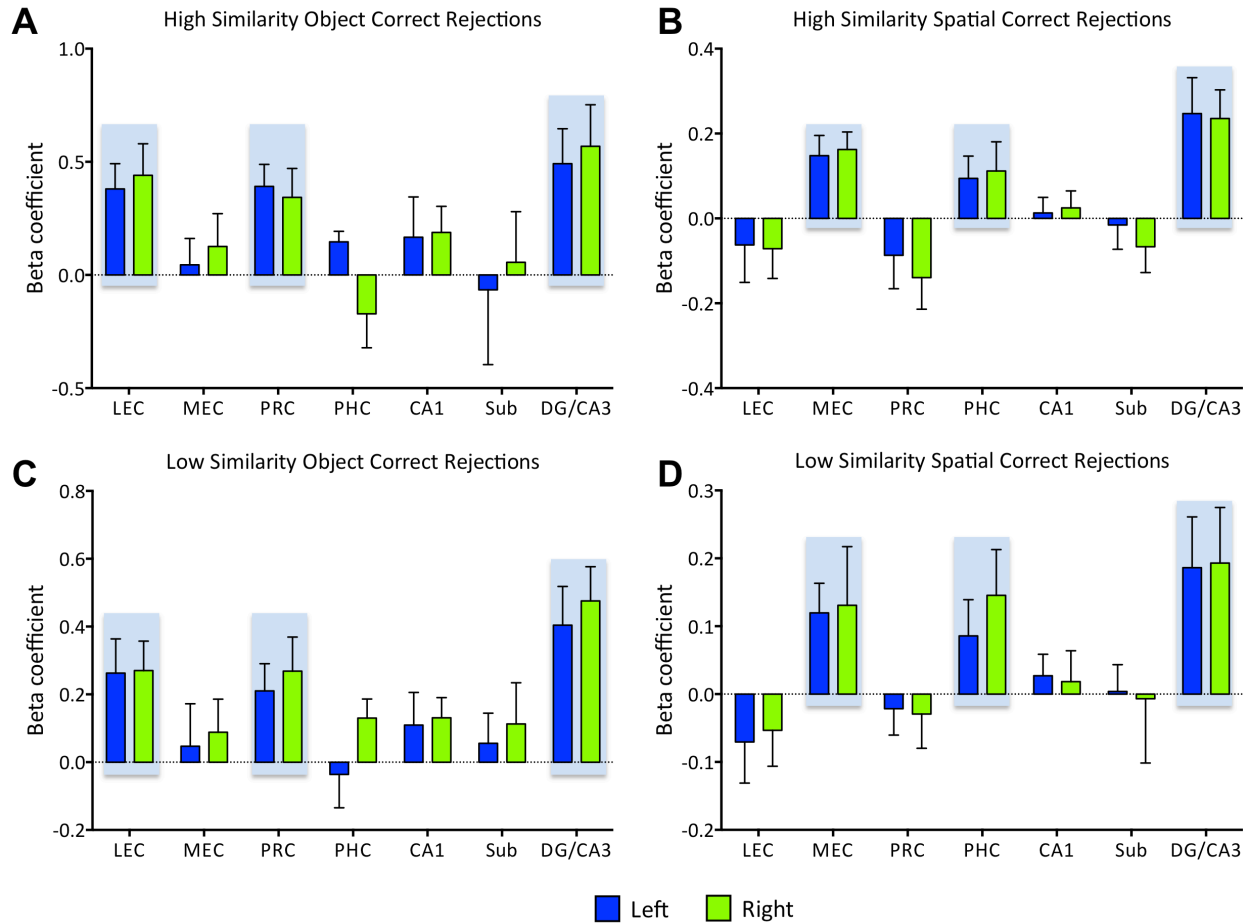


Fig S5. Medial temporal lobe subregion and hippocampal subfield responses during lure correct rejections. (A) Responses on high similarity object correct rejections showing positive responses in LEC, PRC, and DG/CA3; (B) Responses on high similarity spatial correct rejections showing positive responses in MEC, PHC, and DG/CA3; (C) Responses on low similarity object correct rejections showing positive responses in LEC, PRC, and DG/CA3; (D) Responses on low similarity spatial correct rejections showing positive responses in MEC, PHC, and DG/CA3. Data are largely consistent across both hemispheres and across levels of similarity. Abbreviations: LEC: lateral entorhinal cortex, MEC: medial entorhinal cortex, PRC: perirhinal cortex, PHC: parahippocampal cortex, Sub: subiculum, DG: dentate gyrus.

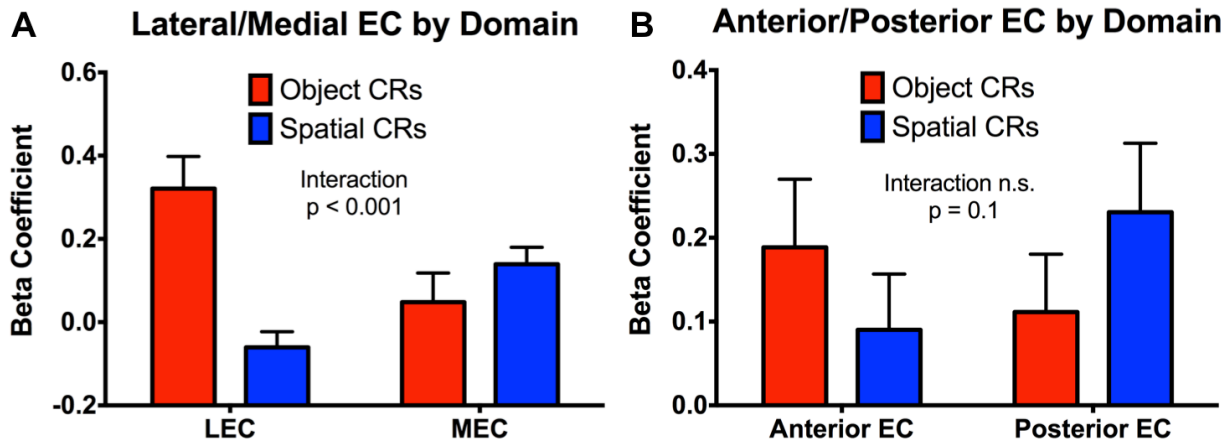


Fig S6. Object vs. Spatial correct rejections as a function of lateral/medial and anterior/posterior segmentations of the EC. (A) A repeated measures ANOVA in EC with a lateral/medial division revealed a significant interaction between region and trial type. (B) The same ANOVA with an anterior/posterior division revealed a marginal, but not significant interaction.

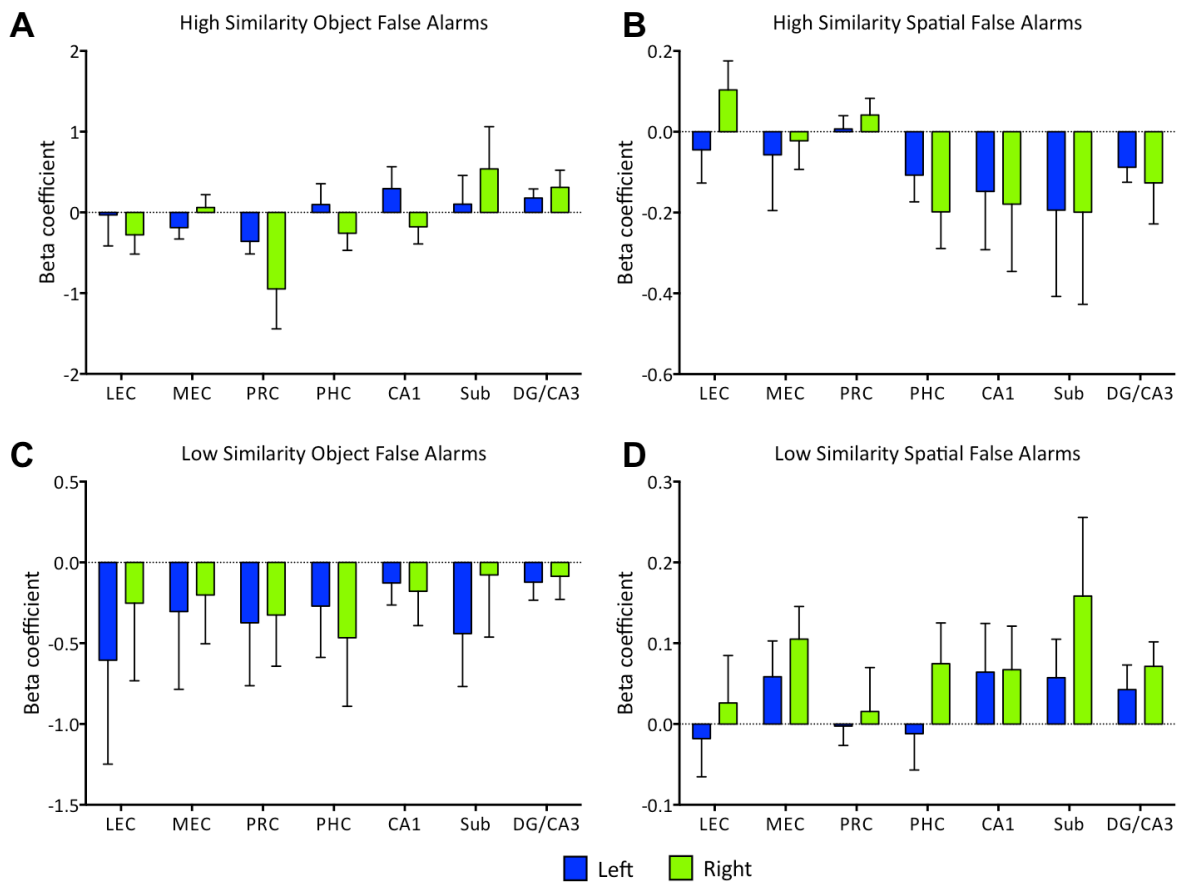


Fig S7. Medial temporal lobe subregion and hippocampal subfield responses during lure false alarms. Due to myriad possible influences on the behavioral result of a false alarm, neural data during these trials are themselves difficult to interpret. Nonetheless, in comparison to other trial outcomes such as correct rejections, the data can inform understanding of the dynamic range of responses within a region. (A) Responses on high similarity object false alarms. (B) Responses on high similarity spatial false alarms. (C) Responses on low similarity object false alarms. (D) Responses on low similarity spatial false alarms. Abbreviations: LEC: lateral entorhinal cortex, MEC: medial entorhinal cortex, PRC: perirhinal cortex, PHC: parahippocampal cortex, Sub: subiculum, DG: dentate gyrus.

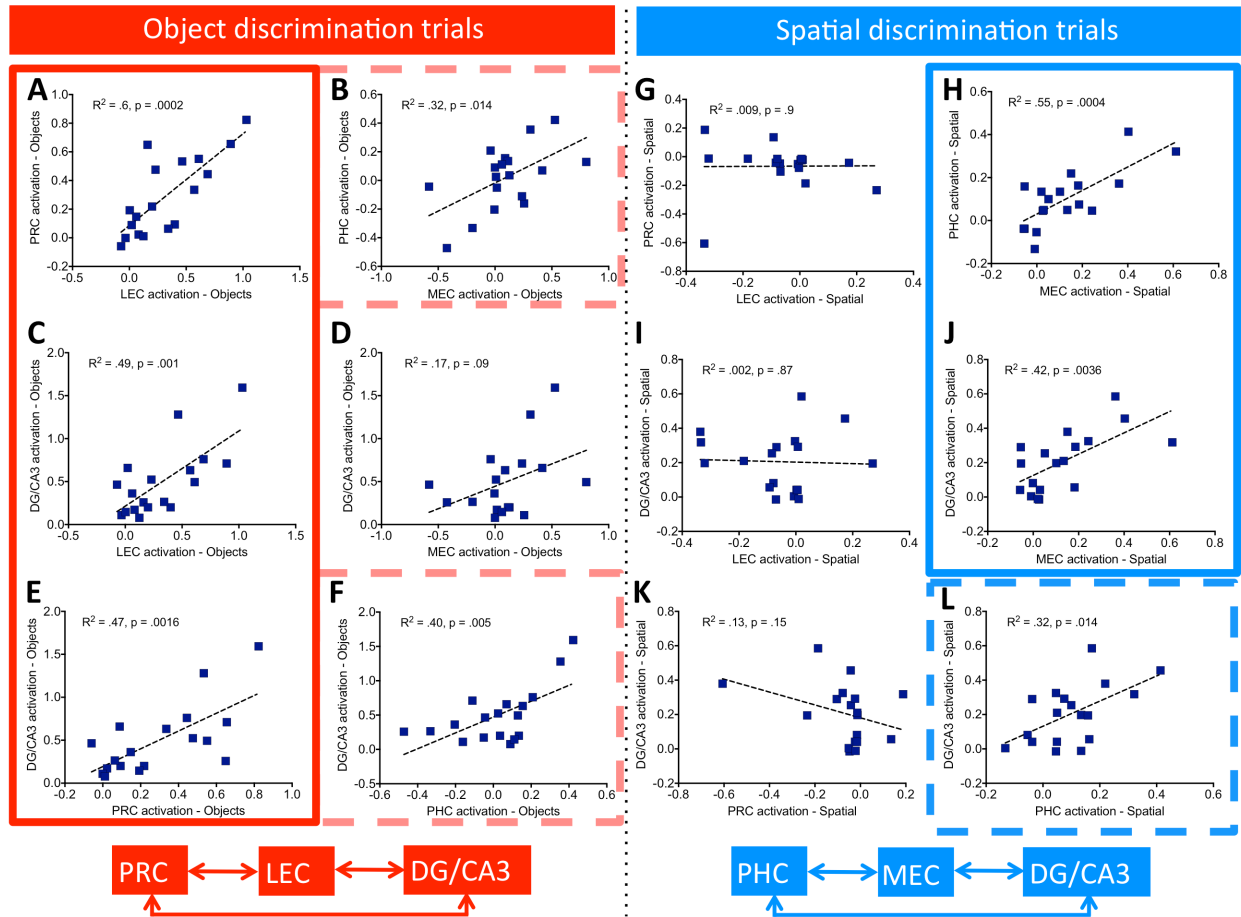


Fig S8. Individual subject contributions to regional correlations. (A,C,E) show pairwise functional correlations between the three regions making up the hypothesized “object” pathway (LEC, PRC, DG/CA3) during object lure correct rejection trials showing strong coupling among these regions; (B,D,F) show pairwise functional correlations between the three regions making up the hypothesized “spatial” pathway (MEC, PHC, DG/CA3) during object lure correct rejection trials showing less correlated activity compared to the object pathway, though perhaps some functional involvement; (G,I,K) show pairwise functional correlations between the three regions making up the hypothesized “object” pathway (LEC, PRC, DG/CA3) during spatial lure correct rejection trials showing virtually no coupling; (H,J,L) show pairwise functional correlations between the three regions making up the hypothesized “spatial” pathway (MEC, PHC, DG/CA3) during spatial lure correct rejection trials showing correlated activity between MEC and PHC as well as between MEC and DG/CA3. The figures at the bottom graphically illustrate the networks that are correlated during object and spatial discrimination, which are consistent with our predictions. The 12 comparisons were corrected using Holm’s sequentially-rejective Bonferroni correction, with an initial critical alpha of $p < 0.0042$. Correlations highlighted with solid lines are significant according to this conservative critical corrected alpha. Dashed lines highlight correlations that are significant at $p < .05$, uncorrected.

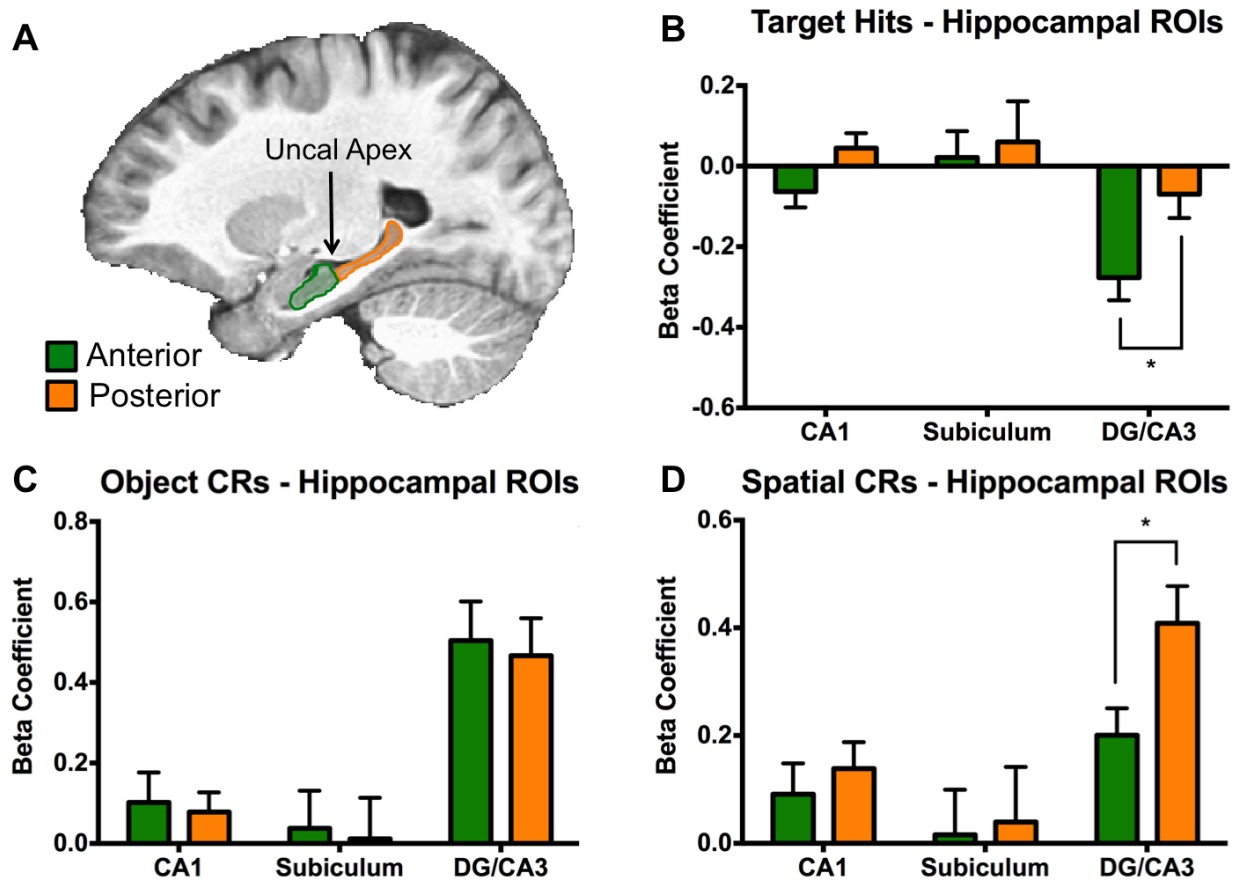


Fig. S9. Subregional activity as a function anterior/posterior hippocampal segmentation. (A) We segmented hippocampal ROIs into anterior and posterior segments using the uncal apex as an anatomical landmark (Poppenk et al., *Trends in Cognitive Sciences* 2013). This is a visualization of the anterior/posterior boundary used to delineate subfields along the hippocampal axis. Anterior hippocampal data are displayed in green, and posterior data are displayed in orange. (B) Activity in anterior DG/CA3 was more diminished during target hits than in posterior DG/CA3. (C) No significant differences were observed along the hippocampal longitudinal axis during object correct rejections. (D) During spatial correct rejections, posterior DG/CA3 was significantly more engaged than anterior DG/CA3.

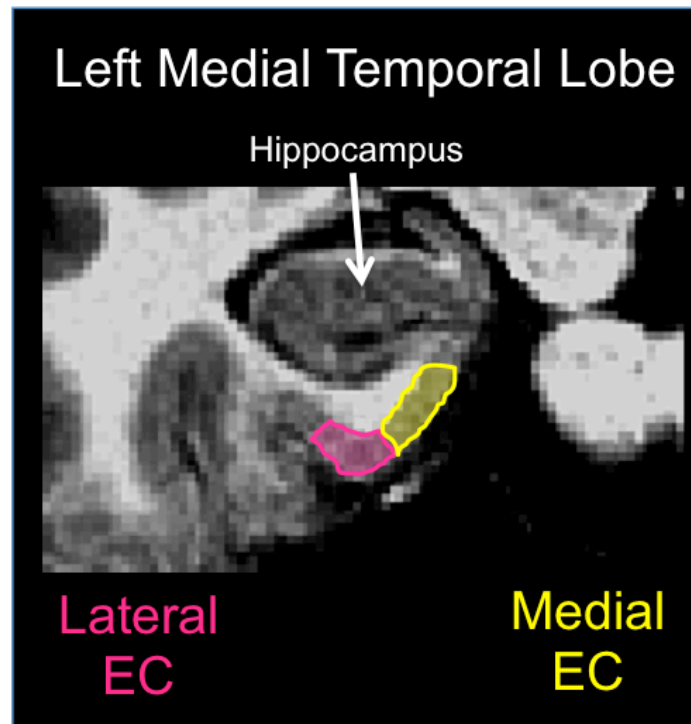


Fig S10. Example segmentation of LEC and MEC in a representative slice of the left MTL. MEC is displayed in yellow and LEC is displayed in pink. Segmentation of the EC was carried out by bisecting into medial and lateral portions using the lateral cortical fold forming the apex of the lower bank of the collateral sulcus as a guideline for approximating a boundary. Additionally, we attempted to bisect the EC such that the medial and lateral ROIs would be designated roughly equal portions of the overall volume of the EC. The line of division was drawn medially and roughly parallel to the apex of the white matter and perpendicular to the entorhinal cortical surface. As noted in the main text, this segmentation approach, while anatomically informed, is not defined by cytoarchitecture or gene expression.

Table S1. Response proportions across all trial types (N=18).

	No Change	Object Change	Location Change	New Object
Target	0.67	0.11	0.14	0.08
Hi-Sim Object Lure	0.29	0.38	0.22	0.11
Low-Sim Object Lure	0.20	0.52	0.14	0.13
Hi-Sim Spatial Lure	0.34	0.15	0.39	0.12
Low-Sim Spatial Lure	0.20	0.06	0.59	0.15
Foil	0.01	0.09	0.06	0.86