Supporting Online Material:

Materials and methods

Subjects

Nineteen right-handed healthy volunteers (10 female) with a mean age of 25.05 (range 18-38) were recruited from the Johns Hopkins Community. One participant was excluded from the study due to inability to discriminate the stimuli as a result of vision problems. Written consent was obtained from all participants and participants were paid for their participation.

Materials and Procedures

Task stimuli consisted of 1,158 pictures of common namable objects. This included 144 triads of slightly different pictures of the same object (432 total) as well as unrelated single pictures of objects used as foils (726 total). Only the first and second member of each triad was used in analysis (see below). Stimuli were displayed using a back-projection screen and the Cogent 2000 toolbox (www.fil.ion.ucl.ac.uk) for Matlab.

All subjects completed a single scan session with eight runs per session. Each run of 108 trials consisted of 18 randomly chosen triads along with 54 randomly chosen unrelated foils. Within each triad, there were three similar stimuli (versions A, B, and C; see Fig. 1) that could be presented in several orders. One third of the triads consisted of the trial type sequence AAA (same version presented three times), one third consisted of the trial type sequence ABC (different version presented each time) and finally one third

of the triads consisted of the trial type sequence ABA. On each trial, a presented object could thus be 1) new, 2) a repetition of a previously shown object, or 3) a slightly different version of a previously shown object. The use of stimulus triads in this study rather than pairs was meant to parallel a related study in our lab and allow for a direct comparison between the two. An analysis of the third trial is not presented here, however as the third trails represent an unknown mix of signals as. On each presentation there is a probability that the stimulus will be perceived as new, old, or similar and a probability that it will be encoded in such a way as to support later recognition as new, old, or similar. By the third presentation, these probabilities become strongly confounded, diluting differences between conditions and perhaps inducing artifacts as well. Therefore, for the purposes of this study, only the effects of the first presentation of a stimulus, the effects of any repetition and the effects of any lure stimulus were analyzed.

Each run resulted in 18 first presentation trials, 12 lure trials and 6 repetition trials. All trials were presented in pseudo random order with the limitation that a repeat or a lure trial would be presented within approximately 30 trials of each other. Each stimulus was presented for 2500 ms with a 500 ms inter-trial interval resulting in a total time of five minutes and 24 seconds per run.

For each stimulus, subjects were asked to determine if the object was predominantly for use as an indoor item or an outdoor item. These instructions were displayed on the screen before each scan block and no further information about the purpose of the study was given to the subject. Responses were made by means of button boxes under the index finger of each hand. Behavioral responses for each item were recorded but were not analyzed in this study.

MRI Data acquisition

Imaging parameters were based on methods previously published (*1*). Imaging was conducted on a 3 Tesla Philips scanner equipped with a SENSE (sensitivity encoding) head coil at the F. M. Kirby Research Center for Functional Brain Imaging at the Kennedy Krieger Institute (Baltimore, MD). As a parallel imaging technique, SENSE was used to acquire the data with significantly reduced acquisition time and reduced distortion attributable to magnetic susceptibility (*2*). Functional echoplanar images were collected using a high-speed echoplanar single-shot pulse sequence with an acquisition matrix of 64 x 64, an echo time of 30 ms., a flip angle of 70°, a sense factor of 2, and an in-plane acquisition resolution of 1.5 x 1.5 mm. Each functional run consisted of a total of 216 volumes with a TR of 1.5 seconds and each volume consisted of 19 oblique 1.5 mm thick axial slices with no gap oriented along the long axis of the hippocampus, and centered to include the hippocampus and most of the parahippocampal gyrus. A total of four dummy scans were completed before data acquisition began to allow for stabilization of the MR signal.

For anatomical localization and cross participant alignment, a standard whole brain, three-dimensional magnetization-prepared rapid gradient echo (MP-RAGE) pulse sequence was acquired. This structural scan consisted of 150 oblique axial slices with 1 x 1 x 1 mm voxels in the same orientation as the functional images.

fMRI Data Analysis

Data analysis was performed using the Analysis of Functional Neuroimages (AFNI) software (*3*). Functional imaging data was first coregistered in three dimensions to the standard whole brain anatomical data. Functional data was also coregistered through time to reduce the effect of any head motion.

Six vectors were defined to represent the first presentation of a stimulus (1^{st}), the first repetition of a stimulus (repeat 1), the second repetition of a stimulus (repeat 2), the first presentation of a similar but slightly different stimulus (lure 1), the presentation of a second similar but slightly different stimulus (lure 2) and the presentation of an unrelated foil stimulus (unrelated). These vectors were subsequently entered into a general linear model (GLM) to model each subject's functional data using a deconvolution approach (http://afni.nimh.nih.gov/pb/dist/doc/manuals/3dDeconvolve.pdf) treating the unrelated stimuli as the baseline. The resulting statistical maps of fit coefficients represent the difference in activity between each of the trial types and the baseline consisting of the unrelated presentations. The statistical maps were then smoothed using a Gaussian filter with a full-width-half-maximum of 3 mm to help account for variations in individual functional anatomy.

Cross Subject Alignment

For cross participant alignment, Region of Interest Large Deformation Diffeomorphic Metric Mapping (ROI-LDDMM) was used. This method has been previously used in our lab and described in detail elsewhere (*1,4*). Briefly, ROI-LDDMM creates a 3D vector field that smoothly transforms images between coordinate systems so that connected sets remain connected, disjoint sets remain disjoint, and sub manifold structures are

preserved. This alignment procedure consisted of several steps. First, the anatomical as well as the functional scans were normalized to the Talairach atlas (*5*) using AFNI. This provided a rough initial alignment and removed any large spatial shifts between subjects, thus improving the performance of the realignment algorithm ROI-LDDMM. Regions of interest were hand segmented in 3D using the Talairach transformed structural MP-RAGE images and these hand segmentations (labels identifying each structure) rather than grayscale images are used as the basis for alignment. Although the least amount of alignment error in cross subject alignment is observed when hand segmentations of the subfields of the hippocampus are available, findings described by Kirwan et al. (*1*) show that accurate subfield-level cross subject alignment (of CA1, CA3/dentate gyrus and subiculum) can be achieved by merely providing a single segmentation for the hippocampus.

Therefore regions included bilateral hippocampus, temporal polar, perirhinal, entorhinal and parahippocampal cortices according to the landmarks described by Insausti et al. (*6*). Insausti et al. (6) provide a detailed description of the delineation of the collateral sulcus and parahippocampal gyrus into an inferotemporal polar portion of perirhinal cortex, perirhinal cortex, and entorhinal cortex. This description, based on a comparison between histology and MRI images, can be used to identify these regions in the face of individual anatomical variations (e.g., length and depth of the collateral sulcus, splits in the sulcus, etc.) Briefly, the inferotemperopolar cortex was defined as the cortex rostral to the appearance of the gyrus of Schwalbe as well as the cortex in the medial aspect of the MTL between and including the gyrus of Schwalbe and the inferior temporal sulcus. The perirhinal cortex was defined as the cortex between and including

the gyrus of Schwalbe and the lateral edge of the collateral sulcus caudal to the appearance of the collateral sulcus and continued for approximately 2 mm caudal to the appearance of white matter entering the MTL. The border between the entorhinal cortex and the perirhinal cortex depended on the depth of the collateral sulcus as described in detail by Insausti et al. (*6*). If the collateral sulcus was regular, the border between the entorhinal and perirhinal cortex was defined as the midpoint of the medial bank. The caudal border of the entorhinal cortex was defined approximately 2 mm caudal to the disappearance of the Hippocampal uncus. Extending from Insausti et al. (6), the parahippocampal cortex was defined bilaterally as the portion of the parahippocampal gyrus caudal to the perirhinal cortex and rostral to the splenium of the corpus collosum (Fig. S2) (see also *7*-*9*). The anatomically defined ROIs were subsequently used to determine the ROI-LDDMM 3D vector field transformation required for each subject using a central tendency modal model developed by our lab as the target. The resulting ROI-LDDMM vector field transformation was then applied to the statistical maps for that subject. A central tendency modal model with full subfield segmentation of the CA1, CA3/dentate gyrus and subiculum developed by our lab was then used as a template to determine the anatomical location of areas of activation obtained from group analyses at the subfield level.

Supporting Figures

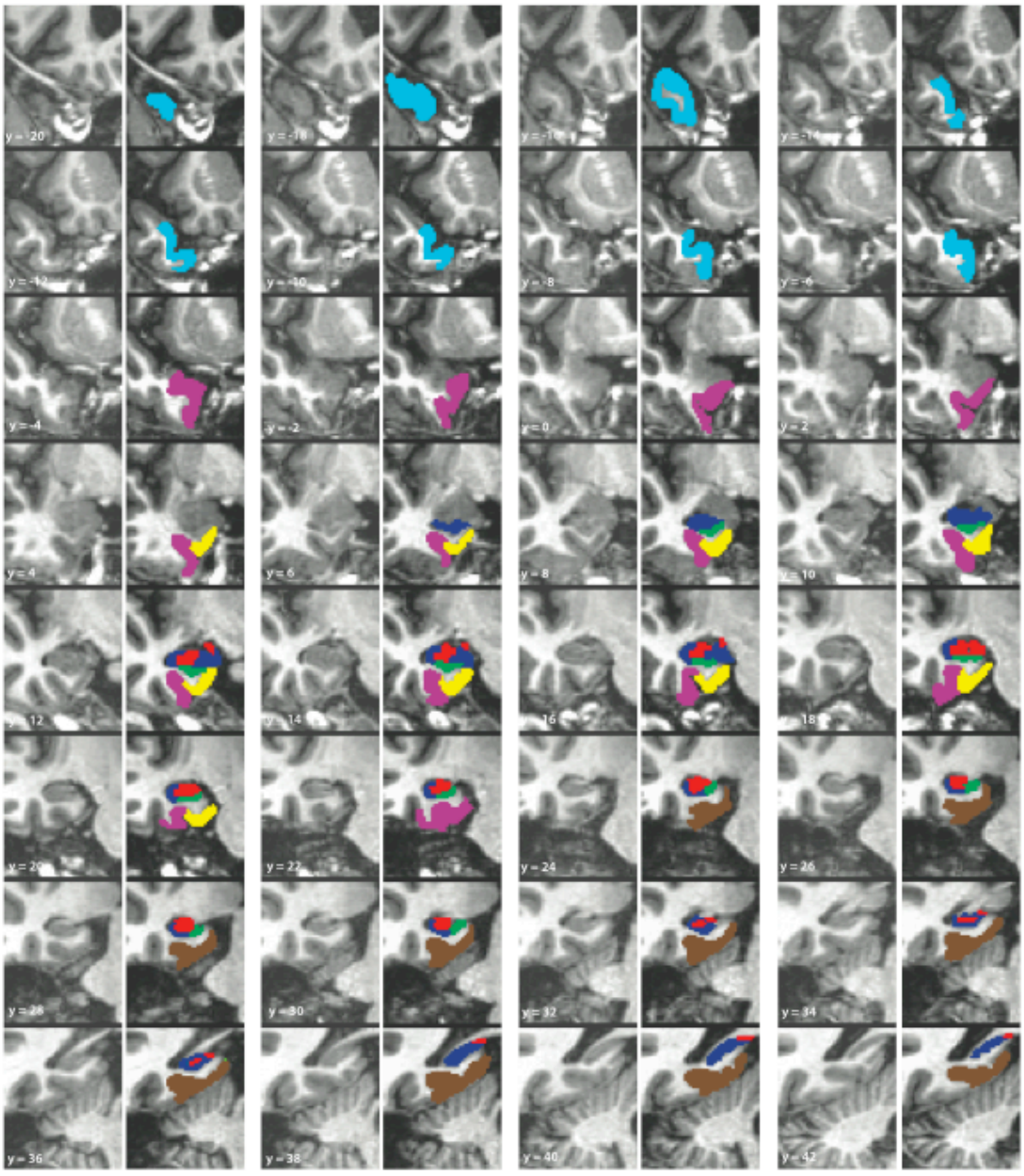

Figure S1: Complete segmentation of the MTL throughout the AP-axis of a single subject. Images are presented in column pairs. The left image shows the section of the MTL while the right image shows the segmentations for that section (light blue =

Temporal polar cortex; magenta = Perirhinal cortex; yellow = Entorhinal cortex; brown = Parahippocampal cortex; blue = CA1; red = CA3/DG and green = Subiculum). Images from anterior to posterior are presented from left to right in 2 mm steps. The approximate Talairach y-coordinate is provided for each of the image pairs.

References for supporting online material

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