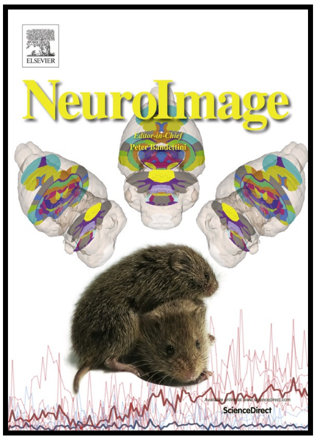
Article:

Sormaz, Mladen, Jefferies, Elizabeth orcid.org/0000-0002-3826-4330, Bernhardt, Boris C et al. (6 more authors) (2017) Knowing what from where:Hippocampal connectivity with temporoparietal cortex at rest is linked to individual differences in semantic and topographic memory. Neuroimage. pp. 400-410. ISSN 1053-8119

https://doi.org/10.1016/j.neuroimage.2017.02.071



www.elsevier.com

Knowing what from where: Hippocampal connectivity with temporoparietal cortex at rest is linked to individual differences in semantic and topographic memory

Mladen Sormaz, Elizabeth Jefferies, Boris C. Bernhardt, Theodoros Karapanagiotidis, Giovanna Mollo, Neda Bernasconi, Andrea Bernasconi, Tom Hartley, Jonathan Smallwood

PII: S1053-8119(17)30182-9
DOI: http://dx.doi.org/10.1016/j.neuroimage.2017.02.071
Reference: YNIMG13856

To appear in: *NeuroImage*

Received date: 1 November 2016
Revised date: 10 February 2017
Accepted date: 24 February 2017

Cite this article as: Mladen Sormaz, Elizabeth Jefferies, Boris C. Bernhard Theodoros Karapanagiotidis, Giovanna Mollo, Neda Bernasconi, Andre Bernasconi, Tom Hartley and Jonathan Smallwood, Knowing what from where Hippocampal connectivity with temporoparietal cortex at rest is linked t individual differences in semantic and topographic memory, *NeuroImag* http://dx.doi.org/10.1016/j.neuroimage.2017.02.071

Knowing what from where: Hippocampal connectivity with temporoparietal cortex at rest is linked to individual differences in semantic and topographic memory☆

Mladen Sormaz[1*], Elizabeth Jefferies, Boris C. Bernhardt[2,31], Theodoros Karapanagiotidis[1], Giovanna Mollo[1], Neda Bernasconi[32], Andrea Bernasconi[33], Tom Hartley[1] and Jonathan Smallwood[1]
[1]Department of Psychology and York Neuroimaging Centre, University of York, Heslington, York, United Kingdom
[2]Multimodal Imaging and Connectome Analysis Lab, Montreal Neurological Institute, McGill University, Montreal, QC, Canada
[3]Neuroimaging of Epilepsy Laboratory, Montreal Neurological Institute, McGill University, Montreal, QC, Canada
mladen.sormaz@york.ac.uk
beth.jefferies@york.ac.uk
boris.bernhardt@gmail.com
tk710@york.ac.uk
giovanna.mollo@york.ac.uk
neda.ladbon-bernasconi@mcgill.ca
andrea@bic.mni.mcgill.ca
tom.hartley@york.ac.uk
jonny.smallwood@york.ac.uk
[*]Correspondence to: Department of Psychology, University of York, England, YO10 5DD.

Abstract

The hippocampus contributes to episodic, spatial and semantic aspects of memory, yet individual differences within and between these functions are not well-understood. In 136 healthy individuals, we investigated whether these differences reflect variation in the strength of connections between functionally-specialised segments of the hippocampus and diverse cortical regions that participate in different aspects of memory. Better topographical memory was associated with stronger connectivity between lingual gyrus and left anterior, rather than posterior, hippocampus. Better semantic memory was associated with increased

---

[☆] Telephone numbers: all authors at University of York : 01904 323190.
[1] Tel.: +514 398 3044.
[2] Tel.: +514 398 4733.
[3] Tel.: +514 398 3361.

connectivity between the cuneus/precuneus and left, rather than right, posterior hippocampus. Notably, we observed a double dissociation between semantic and topographical memory: better semantic memory was associated with stronger connectivity between left temporoparietal cortex and left anterior hippocampus, while better topographic memory was linked to stronger connectivity with right anterior hippocampus. Together these data support a division-of-labour account of hippocampal functioning: at the population level, differences in connectivity across the hippocampus reflect functional specialisation for different facets of memory, while variation in these connectivity patterns across individuals is associated with differences in the capacity to retrieve different types of information. In particular, within-hemisphere connectivity between hippocampus and left temporoparietal cortex supports conceptual processing at the expense of spatial ability.

Keywords
Hippocampus, resting state, semantic, topographic, episodic, large scale dataset

Introduction

Episodic memory involves binding objects in time and space to determine when and where events occurred. In humans, the hippocampus is important for this process: patients with hippocampal lesions show amnesia (e.g. Scoville & Milner, 1957, Spiers, Maguire, & Burgess, 2001) and neuroimaging investigations highlight the hippocampus as important in recollection (for a review see Rugg & Vilberg, 2013). The hippocampus also supports spatial and meaning-based relations beyond episodic memory. For example, single cell recordings in rodents, as well as neuroimaging investigations of navigation in humans, reveals a role for this structure in representing the current location in space (for a review see Buzsáki & Moser, 2013). The hippocampus and the medial temporal lobe work in tandem, forming semantic relationships based on associative learning (Manns, Hopkins, & Squire, 2003; Ryan, Cox, Hayes, & Nadel, 2008; Greenberg & Verfaellie, 2010; Constantinescu, O'Reilly, & Behrens, 2016). Although the role of hippocampus in humans in episodic memory is well documented, it may play a broader role in acquiring and maintaining relationships between objects and spatial locations, processes critical for episodic memory (for a recent review, see Moscovitch, Cabeza, Winocur, & Nadel, 2016).

The hippocampus forms connections with other regions of cortex that could provide the basis for its role in memory, since they would allow it to link together information about objects, places, faces, words, actions and emotional valence at encoding, and reactivate these aspects of knowledge during recall (e.g. Horner, Bisby, Bush, Lin, & Burgess, 2015). It is increasingly recognised that differences in connectivity along the posterior-anterior axis of the hippocampus could give rise to functional specialisation (Poppenk, Evensmoen, Moscovitch, & Nadel, 2013; Strange, Witter, Lein, & Moser, 2014; Ranganath & Ritchey, 2012; Chase et al., 2015). For example, connections from the posterior hippocampus to occipital and parietal regions provide perceptual information about objects and places (Nadel & Peterson, 2013; Bird & Burgess, 2008; Hassabis & Maguire, 2011). In contrast, anterior hippocampus is strongly connected to ventromedial prefrontal cortex and the anterior temporal lobes, providing conceptual and schematic elements of memory (Patterson, Nestor, & Rogers, 2007; Jefferies, 2013, Rice, Ralph, & Hoffman, 2015, Peelen & Caramazza, 2012). More recently, it has also been noted that there may be a division of labour between left and right hippocampus, with the left hemisphere showing greater connectivity to limbic regions (Robinson, Salibi, & Deshpande, 2016), although the conclusions about hemispheric differences are largely driven by structure rather than evidence of differential function.

The current study examined the hypothesis that the function of hippocampal segments is reflected in their functional connectivity with neocortical regions. Our study builds on prior work that demonstrated connectivity from the MTL at rest to regions of visual cortex was associated with endorsing visuo-spatial episodic details in autobiographical memory while remembering semantic information (factual knowledge) was linked to MTL coupling to inferior and middle prefrontal regions (Sheldon, Farb, Palombo, & Levine, 2016).

We collected resting-state functional MRI data in a large cohort of individuals who subsequently performed a battery of cognitive tasks, including measures of semantic, episodic, and topographical memory. We calculated spatial maps for each individual that described patterns of differential functional connectivity along both the sagittal and anterior-posterior axis in the hippocampus. Following this we established (i) whether hippocampal sub regions were differentially connected to areas of neocortex implicated in semantic, spatial and episodic aspects of memory when regressed with behavioural performance in these memory tasks,; (ii) if dissociations *between* different memory tasks might reflect differential connectivity between hippocampal sub regions with distinctive functions and neocortical areas that support memory retrieval across domains, such as temporoparietal cortex; (iii) which types of cognitive task regions highlighted by this differential hippocampal functional connectivity were related to using a meta-analytic decoding approach. In this way, we tested critical predictions of an account of hippocampal function that assumes that connections to diverse neocortical areas allow information of different types to be bound together in memory.

Method

Participants

A group of 136 participants (81 females; mean ±SD age = 20.4 ±2.5 years) were recruited for this study. They were right handed, native English speakers, with normal/corrected vision and no history of psychiatric or neurological illness. This cohort was acquired from the undergraduate and postgraduate student body at the University of York. All volunteers provided informed written consent and were paid either £80 or given course credit for their participation.

Procedure

Participants underwent MRI scanning followed by three 2-hour long behavioural testing sessions where they completed a battery of computer based tasks within a week of the scan. This study was approved by the University of York Neuroimaging Centre and by the University of York Department of Psychology ethics committees. For inclusion in the fMRI analysis participants were required to have taken part in the Paired Associate Task (PAT) within 5 days of the fMRI resting state scan and to have reached a performance criterion of 60% correct responses, with a maximum of three repetitions of the recall phase for the entire list of word pairs. 82% of the original cohort (n=165) met this criterion, those who did not were excluded from the study (n = 29).

Design

Our aim was to determine whether across-subject variability in hippocampal functional connectivity (along its anterior-posterior axis and left-right along the sagittal plane) predicts inter-individual differences in memory performance measured across three domains (episodic, topographical, semantic).

Tasks

Participants first took part in an hour long MRI session that included a number of structural MRI scans and a 9 minute functional MRI resting state scan where they simply viewed a central fixation cross on a grey screen.

In the following days participants completed a large battery of tasks as part of a larger cohort study involving seven hours of testing split across 3 separate sessions. Of these measures, three were intended to examine differences in semantic, topographic and episodic memory at issue in the current study. The order that participants completed memory tasks was counterbalanced across and between sessions 1-3. The left hand panel of Figure 1 provides a schematic illustration of the three tasks we used in this study.

Semantic memory: To test semantic ability, participants carried out a relatedness judgment task employing 60 probe words (e.g., *dog*) that were paired with 60 semantically-related words (e.g., *bone*). The word pairs were selected from a larger dataset used in previous experiments (Davey et al., 2015; Krieger-Redwood, 2012). The strength of association between the word pairs was measured using a 7-point Likert scale and ranged between 1.8 – 6.8 (mean 4.5 ± 1.2). Using a 3-alternative force choice (3AFC) paradigm, each trial started with 500 ms blank screen, followed by the three choices presented on the bottom of the screen. After 900 ms, the probe was presented on the top middle section of the screen. Probe and choices remained visible until participants' response or for a maximum of 3s.

Participants were asked to select the word related in meaning with the probe. The distracters of each trial were selected among the targets from other trials ensuring that they were not linked to the probe. The task took approximately 10 minutes to complete. Accuracy percentages were calculated for each participant by summing the number of trials where each participant correctly matched target words to the correct semantically related word.

Topographical memory: The Four Mountains Task (Hartley et al., 2007) provided a measure of topographical memory. Participants viewed a "sample" image for 10 s before selecting the image, from amongst 4 alternatives, which showed the same location as the sample but from a different viewpoint (20 s were allowed for each decision). Lighting conditions, weather and vegetation textures were varied between sample and test to prevent participants from using a simple visual matching strategy. For the same reason, the foil images were comprised of similar landscapes containing some of the same elements (i.e., hills) in different arrangements and no visual features were unique to the target. Participants were asked to select the picture that matched the probe image across 30 trials to assess their ability to recognise a place from its spatial layout as opposed to local visual features. The task took approximately 20 minutes to complete. Accuracy percentages were calculated for each participant by summing the number of trials where each participant correctly matched cue scenes to the correct target scene presented from a different angle.

Episodic memory: Participants also undertook a paired-associate recall task to assess episodic memory as used by Payne et al. (2012). 80 words were selected using University of South Florida (USF) word association, rhyme, and word fragment norms (Nelson, McEvoy, & Schreiber, 2004) to create 40 semantically unrelated cue and target word pairs (e.g. owl –

frame). Both the cue and target words were singular, had high USF concreteness ratings (cues = 5.90 ± 0.61; targets = 5.85 ± 0.41,*t*(39) = 0.39; *p* = .696) and were matched for frequency (cues = 35.10 ± 41.09; targets = 40.73 ± 55.26, *t*(39) = -4.71; *p* =.640), word length (cues = 5.18 ± 1.34; targets = 5.15 ± 1.05, *t*(39) = 0.09; *p* =.933) and number of syllables (cues = 1.45 ± 0.68; targets = 1.55 ± 0.60, *t*(39) = -0.73; *p* = .472). There were no pre-existing forward or backward associated relationships between any of the words, reducing the likelihood of erroneous associations between words in separate pairs.

During an initial learning phase, participants were presented with the unrelated words pairs, one at a time for 5 seconds each. Encoding was followed by a recall phase during which they attempted to recall the second word from the first word in the pair; they had 12 seconds for each trial and received feedback after each response. If there was no response or an error, the feedback included the correct match. Participants were required to reach a performance criterion of 60% correct responses, with a maximum of three repetitions of the recall phase for the entire list of word pairs. 82% of the original cohort met this criterion, those who did not were excluded from the study (n = 29). Episodic recall was then tested (without feedback) immediately and after a delay (median = 1 day, range = 1-5 days). In both sessions, participants provided a confidence rating about each of their responses using a 7-point Likert scale, although we do not analyse these data here. Only the delayed recall scores were used for the regression with resting-state connectivity. The task took approximately 10 minutes to complete. Accuracy percentages were calculated for each participant by summing the number of trials where each participant correctly matched cue words to the correct target word that they had learned in a previous encoding session.

Image acquisition

MRI acquisition: Structural and functional data were acquired using a 3T GE HDx Excite MRI scanner utilising an eight-channel phased array head coil (GE) tuned to 127.4 MHz, at the York Neuroimaging Centre, University of York. Structural MRI acquisition in all participants was based on a T1-weighted 3D fast spoiled gradient echo sequence (TR = 7.8 s, TE = minimum full, flip angle= 20°, matrix size = 256 x 256, 176 slices, voxel size = 1.13 x 1.13 x 1 mm). Resting-state activity was recorded from the whole brain using single-shot 2D gradient-echo-planar imaging (TR = 3 s, TE = minimum full, flip angle = 90°, matrix size = 64 x 64, 60 slices, voxel size = 3 x 3 x 3 mm^3, 180 volumes). A FLAIR scan with the same orientation as the functional scans was collected to improve co-registration between subject-specific structural and functional scans.

Region of Interest Selection and Mask Creation: The right hand panel of **Figure 1** illustrates the masks that we used to describe the regions of interest (ROIs) used in this study. We selected anterior and posterior regions of the hippocampus based on statistical probabilistic anatomic maps of manual hippocampal segmentations, carried out in MNI space in 30 healthy participants following a previously established protocol (Bernasconi et al., 2003) according to anatomical landmarks described by Duvernoy (1988). Hippocampal probabilistic maps were thesholded at a relatively conservative threshold of 60% to ensure the seed regions contained only core hippocampal voxels. To ensure perfect symmetry across hemispheres for anterior and posterior sections of the hippocampus we first performed a binarisation of the 60% thresholded left and right anterior and posterior hippocampal masks. Following this these masks were mirrored across hemisphere using the dimswap command in

FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Fslutils). Finally we multiplied the mirrored hippocampal masks together with the original hippocampal masks leaving us with equally sized, symmetrical anterior and posterior hippocampal masks across hemisphere.

Data pre-processing and analysis

Resting-state fMRI: Functional and structural data were pre-processed and analysed using FMRIB's Software Library (FSL version 4.1, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT/). Individual FLAIR and T1 weighted structural brain images were extracted using BET (Brain Extraction Tool). Structural images were linearly registered to the MNI-152 template using FMRIB's Linear Image Registration Tool (FLIRT) . The resting state functional data were pre-processed and analysed using the FMRI Expert Analysis Tool (FEAT). The individual subject analysis involved: motion correction using MCFLIRT; slice-timing correction using Fourier space time-series phase-shifting; spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 100 s); Gaussian lowpass temporal filtering, with sigma = 2.8s

We extracted the time series from each of the four hippocampal masks (LA, RA, LP and RP) and used these as explanatory variables in connectivity analyses at the single subject level. In each analysis, we entered 11 nuisance regressors; the top five principal components extracted from white matter (WM) and cerebrospinal fluid (CSF) masks based on the CompCor method (Behzadi, Restom, Liau, & Liu, 2007), six head motion parameters and spatial smoothing (Gaussian) was applied at 6mm (FWHM). WM and CSF masks were generated from each individual's structural image (Zhang, Brady, & Smith, 2001). No global signal regression was performed, following the method implemented in Murphy, Birn, Handwerker, Jones, & Bandettini (2009). The nature and interpretation of correlation in resting state analysis is a matter of a debate that is focused on a lack of clarity regarding what constitutes a correlation of zero (see Murphy et al., 2009). We therefore use the terms 'relatively strongly correlated' and 'relatively weakly correlated' to describe regions whose correlation with the seed region is increased or decreased relative to the average.

Our main analysis involved four steps. First, functional connectivity maps were derived from regions of interest in four key regions of the hippocampus: left anterior hippocampus (LA), left posterior hippocampus (LP), right anterior hippocampus (RA), and right posterior hippocampus (RP). Second, these maps were used to calculate differential connectivity maps along both an anterior-posterior axis and a left-right along the sagittal plane at the individual level. These maps describe for each voxel relative differences in functional connectivity between particular subregions of the hippocampus. The left-right difference maps were calculated separately for the anterior and posterior maps (LA vs. RA, LP vs. RP) and the anterior-posterior differences maps were calculated separately for each hemisphere (LA vs. LP, RA vs. RP). Third, the spatial and functional characteristics of these difference maps were identified by calculating group maps and by performing a meta-analytic decoding using the Neurosynth platform (http://neurosynth.org/). This quantifies the functional terms most commonly associated with each spatial map, allowing us to perform a quantitative reverse inference regarding the most likely associated functions. Fourth, we examined the functional relationship of these maps to different types of memory by calculating their relationship to variation in accuracy for semantic, topographical and episodic memory. For this final step we again performed a meta-analytic decomposition of the resultant maps to aid their interpretation. To maximize the transparency of our analyses, all z maps displayed in this study are freely available at the following URL at Neurovault: /collections/LDPQHHTT/. Furthermore to ensure that our spatial smoothing kernel affect our analysis by smoothing beyond seed regions we replicated our results by conducting a first level analysis with a 0mm smoothing kernel, the corresponding z maps can be found at the following URL at Neurovault: /collections/MSFOMKIP/.

Meta analytic decoding

We compared unthresholded functional connectivity activation profiles to those of previous studies using the Neurosynth decoder (http://www.neurosynth.org/decode/). We decoded functional terms associated with the differential functional connectivity maps produced in our analysis, this was the final step of the analysis and undertaken after all of the fMRI analyses (see Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011 for further details). To produce our word clouds we manually extracted the top ten task descriptions (based on frequency) for each unthresholded z map (we manually excluded the names of brain regions or MRI methods) to generate the word clouds in Figures 2 and 3.

Behavioural regression analysis

We related hippocampal connectivity patterns to inter-individual variations in different types of memory using a multiple regression model, in which the four difference connectivity maps were the dependent variable and z scored accuracy on the three memory tasks (see supplementary table 1) the explanatory variables: (i) Semantic memory, (ii) Episodic memory, and (iii) Topographical memory. We also included mean frame displacement (Power et al., 2014) in our group level regressions to rule out spurious effects. These analyses were carried out using FMRIB's Local Analysis of Mixed Effects (FLAME1). Prior to analyses the behavioural data were z-scored. For each of these multiple regression models, we focused on differential memory effects by calculating contrasts that reflected pair-wise differences for each type of memory (e.g., semantic > episodic memory). For all significant effects, we then computed the correlation between the connectivity measure for each individual and performance on the tasks within the pair separately, to determine the form of differential task effects. To control for multiple comparisons we used a cluster forming threshold of Z = 2.6 and controlled our Type I error rate at an alpha value of $p < .0125$ FWE in order to take account of the number of voxels in the brain as well as the four different regression models we conducted. Following Eklund, Nichols, & Knutsson (2016) we selected these parameters to reduce our likelihood of Type I errors

Results

Behavioural task performance

Participants accuracy across each of the three behavioural tasks suggests that participants did not show floor or ceiling effects in any of the behavioural task accuracy rates; Topographic Memory Accuracy (mean = 65.4%, SD ± 15.6%), Episodic Memory Accuracy (mean = 59.8%, SD ± 23.3%), Semantic Memory Accuracy (mean = 89%, SD ± 7.3%). The mean z scored accuracies for each individual can be seen in supplementary table 1.

Functional subdivisions in hippocampus: Differential connectivity and meta-analytic decoding

Figure 2 presents differential connectivity maps comparing anterior and posterior hippocampus, computed separately for the left and right hemispheres. Anterior regions showed stronger connectivity to ventral regions of medial prefrontal cortex, lateral temporal regions, posterior lateral prefrontal cortex and regions of mid-cingulate cortex (indicated by cool colours). Posterior regions showed greater functional connectivity with anterior dorsolateral prefrontal cortex, fusiform, pre-supplementary motor area, and medial occipital cortices (indicated by warm colours). Neurosynth decoding of the spatial maps for anterior hippocampal maps from both hemispheres provided terms related to emotional processing, and facial expressions. By contrast, posterior maps related to terms associated with working memory and visual processing, revealing a functional dissociation along the anterior-posterior axis.

Figure 3 compares the connectivity of left hippocampus (indicated by cool colours) and right hippocampus (indicated by warm colours), computed separately for anterior and posterior hippocampal subregions. The left posterior hippocampus was more connected to the left posterior inferior frontal gyrus and a posterior region in the lateral temporal lobe. The anterior hippocampus was coupled to the ipsilateral dorso-lateral pre-frontal cortex, angular gyrus, posterior cingulate and lateral temporal lobe. In addition, the right anterior hippocampus was more connected to the left lateral occipital cortex, while the left anterior hippocampus was associated with the right posterior insula. While connectivity was strongest within each of the hemispheres, there were some cross-hemispheric differences. Right vs. left comparisons for posterior hippocampus showed stronger connectivity to a region of posterior cingulate cortex in both hemispheres and regions of dorsal angular gyrus and the pre-supplementary area in the right hemisphere. Regardless of whether the analysis examined anterior or posterior aspects of the hippocampus, decoding the spatial maps associated with the left hemisphere revealed functional terms associated with semantic memory and language (e.g., semantic, language, and word). The right hemisphere maps were associated with more perceptual processes (e.g., visuo-spatial, attention, visual), consistent with a functional dissociation between the left–right hippocampus.

Variation in differential connectivity and their association with memory performance

Having determined patterns of functional specialisation along the anterior-posterior and left–right axes in the hippocampus, we next examined whether these patterns were associated with an individuals' memory performance across semantic, episodic, and spatial tasks. We included the accuracy of each participant on each task as an explanatory variable in a series of multiple regression analyses in which the dependent variables were the four connectivity difference maps of interest (LA > RA, LP > RP, LA > LP and RA > RP). We computed contrasts between pairs of tasks and show significant differential effects in Figure 4 and 5. Table 1 presents the results of the contrasts in the form of a table. Table 2 reports the correlation between these connectivity results and performance on the individual tasks to aid interpretation of differential behavioural effects.

Our analysis yielded three significant results, each of which related hippocampal connectivity to functional specialization in memory. First, we identified a cluster in the lingual gyrus in the left hemisphere whose differential connectivity in anterior-posterior direction discriminated between accuracy in topographic and semantic memory tasks (Figure 4, top row). In our participants, there was a significant correlation between connectivity of the left anterior hippocampus and topographic but not semantic memory (see Table 2). Second, we observed a region of medial parieto-occipital cortex, focused on the cuneus, showing differential left-right connectivity with respect to differences in semantic and episodic memory (Figure 4, bottom row). Better semantic memory performance was associated with stronger coupling of this region to left posterior hippocampus, there was a significant correlation between connectivity of the left posterior hippocampus and semantic but not episodic memory (see Table 2).

Third, we observed a cluster extending from posterior temporal-occipital cortex into the left angular gyrus that showed differential left–right connectivity (Figure 5): coupling between this cluster and the anterior hippocampus related to differences in semantic and topographic memory performance. Individuals with more accurate semantic memory showed greater connectivity to left temporoparietal cortex from left anterior hippocampus. Unlike the prior two results, the reverse correlation was also significant: within-hemisphere connectivity between left anterior hippocampus and left temporoparietal cortex was related to poorer performance on topographic memory (see Table 2). Thus, within-hemisphere integration was associated with good semantic performance but poorer topographic memory (see Figure 5).

As indicated by Table 2 and the scatter plots in Figure 5, the cluster in left temporoparietal cortex uniquely showed a double dissociation between aspects of memory: i.e., participants either showed good semantic and poor spatial performance, or the opposite behavioural profile, depending on whether the left temporoparietal cortex showed more within-hemisphere or cross-hemisphere connectivity. To further understand the significance of this dissociation, we examined the spatial distribution of the cluster with respect to patterns of brain activity that might be expected to occur when engaging in spatial or topographic memory tasks. We overlaid the temporoparietal cluster on forward inference meta-analytic maps produced by Neurosynth for the terms “semantic” and “spatial” (see right hand panel in Figure 5). The cluster overlapped with areas implicated in both semantic (yellow) and spatial memory (cyan), as well as regions common to both meta-analytic maps (white). Thus, within-hemisphere connectivity to left temporoparietal cortex from left hippocampus (implicated in semantic processing) supported semantic retrieval, while stronger connectivity to the same region of left temporoparietal cortex from right hippocampus (implicated in navigation) supported topographic memory.

Discussion

A main goal when characterising brain structure and connectivity is to understand function and behaviour in a given individual. Evidence suggests that processes such as episodic memory, spatial navigation and semantic cognition rely on the interaction between hippocampal subregions and specific cortical targets. Here, we characterised differential functional connectivity patterns from hippocampal segments (anterior-vs-posterior; left-vs-right), related them to specific cognitive functions using both a large-scale meta-analytic decoding and an individual difference analysis that assessed the correlations across-subject variations in performance on topographic, episodic and semantic memory tasks. Overall, our findings suggest divisions of labour within the HC, where behavioural variations differentially related to segment-specific connectivity profiles.

Consistent with a graded view of hippocampal function (Strange et al, 2014; Ranganath & Ritchey, 2012; Chase et al., 2015), we found that changes in the anterior-posterior and left-right connectivity within the human HC was related to differences in both connectivity and had a unique relationship to different aspects of memory. Anterior hippocampus showed stronger connectivity with inferior frontal and lateral temporal cortex: meta-analytic decoding revealed functional labels including emotion, sensori-motor and autobiographical memory. These patterns are consistent with recent evidence demonstrating that anterior hippocampus codes memories with a coarser granularity than occurs towards the posterior extension (Collin, Milivojevic, & Doeller, 2015). In contrast, posterior hippocampal regions were more strongly connected to posterior regions of the neocortex including occipital and parietal cortex. Meta analytic decoding suggested these patterns were related to working memory, and visual and spatial processing. Generally, the HC in each hemisphere was more connected to ipsilateral networks. However, we also identified hemispheric differences in connectivity in lateral prefrontal cortex: connectivity with the left posterior HC was focused on left inferior frontal gyrus, while connectivity with the right posterior HC targeted superior lateral prefrontal regions. Meta-analytic decoding linked the left hemisphere with terms such as “semantic”, “language”, “words”, while the right hemisphere was associated with “attention” and “visual”. These results support contemporary theories suggesting the hippocampus provides a mechanism for binding disparate representations in different cortical regions (Marr, 1971; Damasio, 1989; Teyler & Rudy, 2007; Horner et al., 2015) and learning meaningful configurations across domains – including spatial and conceptual representations (Dusek & Eichenbaum, 1997; Eichenbaum & Cohen, 2004). Moreover, since semantic knowledge reflects more long lasting knowledge of the world around us, the association between anterior HC and these types of process is consistent with the observation that anterior HC maintains traces of prior episodic information for longer than does the posterior HC (Ritchey, Montchal, Yonelinas, & Ranganath, 2015).

It follows from these accounts that individual variations in connections from specific hippocampal regions to diverse cortical areas would be associated with individual differences in performance on tasks tapping hippocampal functions, such as episodic memory, semantic memory and topographic processing. Lesion studies have proved equivocal regarding the role of the HC in different types of memory (Vargha-Khadem et al., 1997; Spiers et al., 2001); some patients with extensive hippocampal lesions retain or continue to acquire good conceptual knowledge (e.g. Rosenbaum et al., 2005) suggesting this structure may not always be necessary to understand the meaning of events around us. Nevertheless, our functional connectivity analysis shows that relative strengths and weaknesses in semantic and topographical tasks in a normal population can be related to differential functional connectivity between specific hippocampal segments and their cortical projection zones in occipital and parietal cortex.

We found three differential task effects: first, better topographical memory was associated with stronger coupling from left anterior HC to lingual gyrus, a region implicated in visual processing. This is consistent with the notion that communication between the HC and occipital and parietal cortex provides specific details regarding locations or objects in the world (Epstein, 2008) and provides a conceptual replication of the observation by Sheldon and colleagues (2016) who found that visuo-spatial features of episodic memory are linked to coupling with regions in the visual cortex. Second, connectivity of the left posterior HC, particularly to cuneus/precuneus, was important for semantic memory as assessed via a relatedness judgments task. Importantly, this association with the left posterior hippocampus builds on prior structural evidence suggesting changing functional specialisation along the sagittal plane within the hippocampus (Robinson, Salibi, & Deshpande, 2016) by showing a functional consequence of this bias is increased semantic memory task performance. These two results show that subregional functional connectivity profiles of the hippocampus with cortical projection zones in medial visual cortex differentially relate to the application of topographic and semantic information in memory.

Our third behavioural result demonstrated a double dissociation: connectivity from left temporoparietal cortex to left anterior hippocampus was associated with better semantic memory, while stronger connectivity from the right hippocampus was associated with better topographic memory. Good semantic performance was therefore related to strong connectivity between left anterior hippocampus, the sub-region maximally implicated in semantic processing (see Figure 3), and a cortical projection zone in temporo-parietal cortex also implicated in semantics (see for example Binder et al, 2009, Seghier, 2012). These findings are consistent with the hypothesised role of the anterior HC in conceptual memory (for reviews Zeidman & Maguire, 2016) as well as the left lateralized nature of semantic cognition more generally (Vigneau et al., 2006; Binder et al, 2009). Since our results are related to aptitude in semantic processing they indicate that the hippocampal activation sometimes observed during semantic tasks may not be due to incidental episodic encoding (Binder et al., 2009a), but instead may reflect a meaningful role in conceptual processing. However, as well as relating to good semantic performance, this pattern of connectivity was linked to poor topographic ability, suggesting there is a division of labour across the left and right-hemisphere portions of HC through it’s connections to a region of left temporoparietal cortex. In other words, the pattern of connectivity of the left and right anterior HC at rest with the region of left temporo-parietal cortex describes individual differences in how effectively participants can use semantic or topographic memory. In line with this proposal, the temporoparietal cluster identified from the behavioural regression analysis overlapped with meta-analytic maps for both “semantic” and “spatial” processing (see Figure 5).

The left temporoparietal cluster linked to both good semantic memory and good topographic performance, is known to integrate information from many different large scale networks (Braga et al, 2013). Left temporoparietal cortex is linked to many different forms of memory retrieval: Angular gyrus (within the default mode network) supports autobiographical memory (Spreng, Mar, & Kim, 2008;Cabeza, Ciaramelli, Olson, & Moscovitch, 2008;Bonnici, Richter, Yazar, & Simons, 2016) and more automatic aspects of semantic retrieval (Binder et al., 2009; Humphreys & Lambon Ralph, 2014, Seghier, 2012). Inhibitory TMS to the left angular gyrus region disrupts the retrieval of detailed conceptual knowledge (Davey et al., 2015b). The superior temporal sulcus is linked to metalizing (Saxe & Kanwisher, 2003), and posterior middle temporal gyrus (at the ventral extent of the cluster) is associated with retrieval of weak semantic associations (Noonan, Jefferies, Visser, & Lambon Ralph, 2013 ; Davey et al., 2015; Davey et al., 2016). Thus, the cluster we identified is well-suited for the allocation of attention to activated memory representations (Cabeza et al., 2011) and maybe important in autobiographical memory because it allows multiple distributed features to be recombined together (Wagner, van Buuren, Bovy, & Fernandez, 2016; Kuhl & Chun, 2014, Wagner et al., 2015, Bonnici et al., 2016). Interestingly, inferior parietal cortex is also strongly associated with spatial attention, especially in the right hemisphere: for example, right-sided damage here often results in spatial neglect hemisphere (Mesulam, 1981) and meta-analytic decoding revealed a contribution to spatial processing in both the left and right. It is possible that a dissociation in the connectivity of left-temporo parietal region with the left and right HC could give rise to individual differences in memory because it reflects differences in how easily hippocampal representations (capturing conceptual and spatial aspects of events, for example) accrue attention.

There are a number of limitations that should be borne in mind when considering the implication of our results. First, our study recorded fMRI while participants were at rest rather than while they performed tasks. By describing how the functional architecture of the hippocampus relates to aptitude on different aspects of memory in a large cohort of healthy individuals, we were able to define the broad functional profile of different segments of hippocampal connectivity. This method, however, is an indirect way of probing the precise role that different patterns of connectivity play in different aspects of memory because the data characterises trait-level differences in performance rather than state-related patterns of connectivity. In the future it will be important to collect measures of neural function, in a similar sized cohort of participants, while they perform tasks tapping different aspects of memory. Such an analysis will also be well suited to identify patterns of hippocampal connectivity that are common across many tasks. Second, the tasks used to assess different types of memory varied on a number of relatively superficial attributes such as reliance on recognition (semantic / topographic) or recollection (episodic), or whether the stimulus was pictorial (topographic) versus based on words (semantic / episodic). Consequently certain features of our results may emerge due to differences in the paradigms, such as the association between the lingual gyrus coupling and topographic memory. Future studies could explore whether functional coupling between the lingual gyrus and the hippocampus is helpful whenever memories have a visual code or whether they are specific to retrieving relationships in space. Critically, however, such accounts cannot explain the double dissociation observed in the association between left and right anterior hippocampus and the left temporoparietal cluster since it distinguished spatial and semantic tasks, which both utilise an alternative forced choice paradigm, and was unrelated to performance on the episodic memory tasks, which shared the same representational code as the semantic memory task (words). Instead of supporting these superficial accounts of our data, the double dissociation between hippocampal connectivity and the left temporoparietal cortex shows that, across individuals, the strength of specific neocortical-hippocampal networks is linked to why some people are good at one aspect of memory and poor at another. Third, future studies may gain more precise accounts of the functions of different types of hippocampal connectivity by using more detailed descriptions of hippocampal architecture using either manual or automatic segmentation techniques (see for example, Kulaga-Yoskovitz et al., 2015). Finally we also acknowledge that there is evidence that gender or biological sex may play a role in abilities in working memory (e.g. Harness, Jacot, Scherf, White, & Warnick, 2008; Hill, Laird, & Robinson, 2014). Although this is not the main focus of the current study, future research may want to investigate whether there are gender differences in functional connectivity related to different memory domains (e.g. episodic, topographic or semantic memory).

In summary, our study has provided evidence that individual variation in connectivity from the HC describes patterns of memory retrieval in a manner that is consistent with a role for this system in bringing together different representational codes in episodic memory. We conclude by considering the implications of our findings for understanding individual variation in autobiographical memory and the role of the hippocampus in cognition more generally. Notably, we found no relationship to paired associate memory, but rather observed differences on the semantic and topographic elements that make up episodic memories, suggesting this process of competition may be most apparent for the elements that make up our autobiographical memories. Real episodic memories link spatial and conceptual information, forming a rich multi dimensional representation of what happened where, and our findings suggest qualitative differences in the details that autobiographical memories include may reflect relative strengths in the connections between different regions of the hippocampus and convergence zones, such as those in temporoparietal cortex. Strong connectivity between left anterior HC and semantic regions may predispose an individual to recall features of an episode that were conceptual in nature, while robust connections between the posterior hippocampus and visual cortex may bias memories towards the arrangement of objects in space. More generally, since the hippocampus is important for many types of thought, biases in connectivity across individuals may influence the nature of the experiences that are generated when people prospect (Schacter, Addis, & Buckner, 2007), mind-wander (Fox, Spreng, Ellamil, Andrews-Hanna, & Christoff, 2016) or consolidate memories (Medea et al., 2016).

Table 1. Clusters of activity that have differential correlations with semantic, topographic and episodic memory

Hem	**connectivity**	**Z**	**x**	**y**	**z**	**total voxels**	**p**
	Left Head vs. Right Head with 4MT score					818	<.001
L	Inferior Temporal Gyrus (TO part)	4.5	-52	-44	12		
L	Lateral Occipital Cortex (superior)	4.0	-54	-64	16		
L	Planum Temporale	3.9	-54	-38	18		
L	Supramarginal Gyrus	3.6	-62	-44	32		
L	Parietal Operculum Cortex	3.6	-42	-38	18		
L	Lateral Occipital Cortex (superior)	3.5	-46	-66	16		
L	Inferior Temporal Gyrus (TO part)	4.5	-52	-44	12		
	Left Head vs. Right Head with RTJ vs. 4MT score					874	<.001
L	Supramarginal Gyrus (posterior)	4.4	-52	-44	12		
L	Lateral Occipital Cortex (inferior)	4.3	-42	-64	12		
L	Lateral Occipital Cortex (superior)	4.2	-56	-70	6		
L	Lateral Occipital Cortex (inferior)	4.1	-54	-66	8		
L	Planum Temporale	3.5	-50	-36	18		
L	Parietal Operculum Cortex	3.4	-42	-38	18		
	Left Tail vs. Right Tail with RJT score					761	.002

R	Intracalcarine Cortex	4.0	12	-68	14		
L	Intracalcarine Cortex	3.7	-8	-80	16		
L	Intracalcarine Cortex	3.7	-10	-76	16		
L	Intracalcarine Cortex	3.5	14	-84	6		
L	Intracalcarine Cortex	3.5	-4	-78	10		
L	Cuneal Cortex	3.3	-10	-72	22		
	Left Tail vs. Right Tail with RJT vs. PAT score					543	.01
R	Lingual Gyrus	4.1	4	-60	2		
R	Intracalcarine Cortex	3.6	10	-68	16		
L	Intracalcarine Cortex	3.2	12	-86	-4		
L	Intracalcarine Cortex	3.2	-6	-78	8		
R	Intracalcarine Cortex	3.2	6	-78	10		
R	Precuneus Cortex	3.2	16	-66	22		
	Left Head vs. Left Tail with 4MT score					1558	<.001
R	Lingual Gyrus	5.5	4	-82	-10		
L	Lingual Gyrus	4.9	-4	-70	-12		
L	Cerebellum	4.6	-2	-62	-8		
R	Lingual gyrus/Occipital Fusiform Gyrus	4.3	12	-74	-14		
L	Lingual Gyrus/Cerebellum	4.3	-2	-66	-8		
R	Lingual Gyrus/Cerebellum	3.9	8	-56	-8		
	Left Head vs. Left Tail with 4MT vs. PAT score					594	.007
L	Lingual Gyrus/Cerebellum	5.1	4	-82	-10		
R	Lingual Gyrus	3.9	-4	-72	-12		
L	Lingual Gyrus	3.3	-4	-58	-8		
R	Lingual Gyrus/Cerebellum	3.2	4	-84	-22		
R	Lingual Gyrus	3.2	8	-58	-6		
L	Cerebellum	3.2	-2	-62	-8		

Table 2. Simple correlations between performance on the different memory tasks and the connectivity identified through a whole brain analysis of the relationship between differential memory performance and differential hippocampal connectivity.

	Cuneus / Precuneus	Lingual Gyrus	Temporoparietal Cortex
	LP>RP	LA>LP	LA>RA
Topographical Memory	0.10	0.40^{***}	-0.21^{*}
Semantic Memory	0.29^{***}	0.00	0.28^{**}
Episodic Memory	-0.165	-0.03	0.04

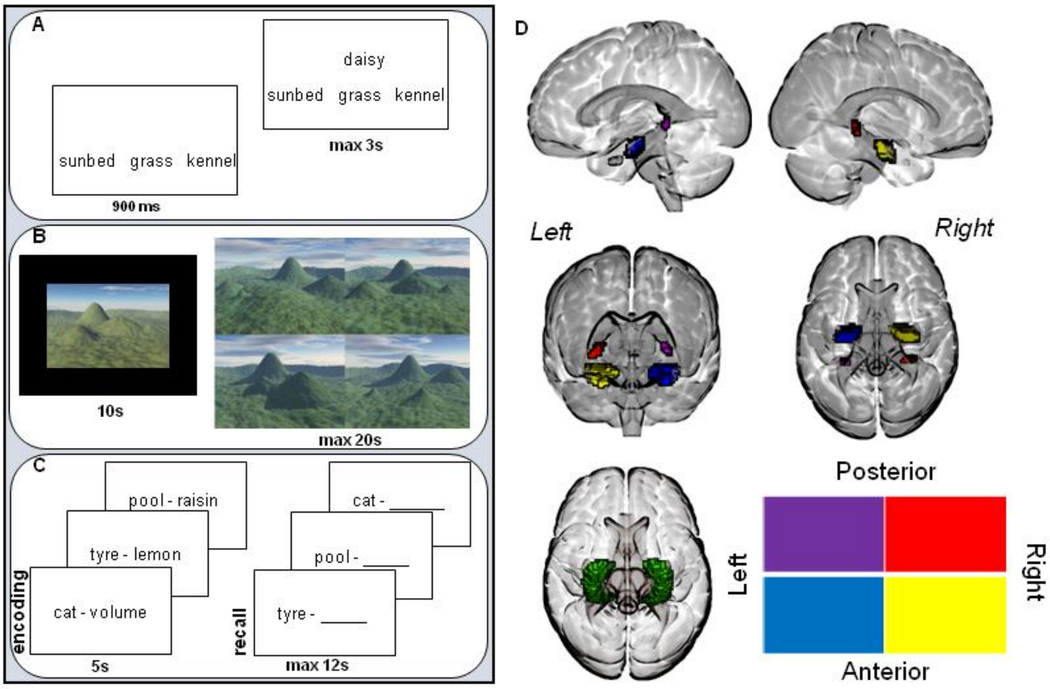


Figure 1. Illustration of the measures of topographical, semantic and episodic memory used in this experiment. The left hand panel illustrates the trial sequence for the tests of (A) Semantic Memory (B) Topographic Memory and (C) Episodic Memory. The right hand panel (D) illustrates how the regions of interest in anterior and posterior regions of the hippocampus in the left and right hemisphere were determined.

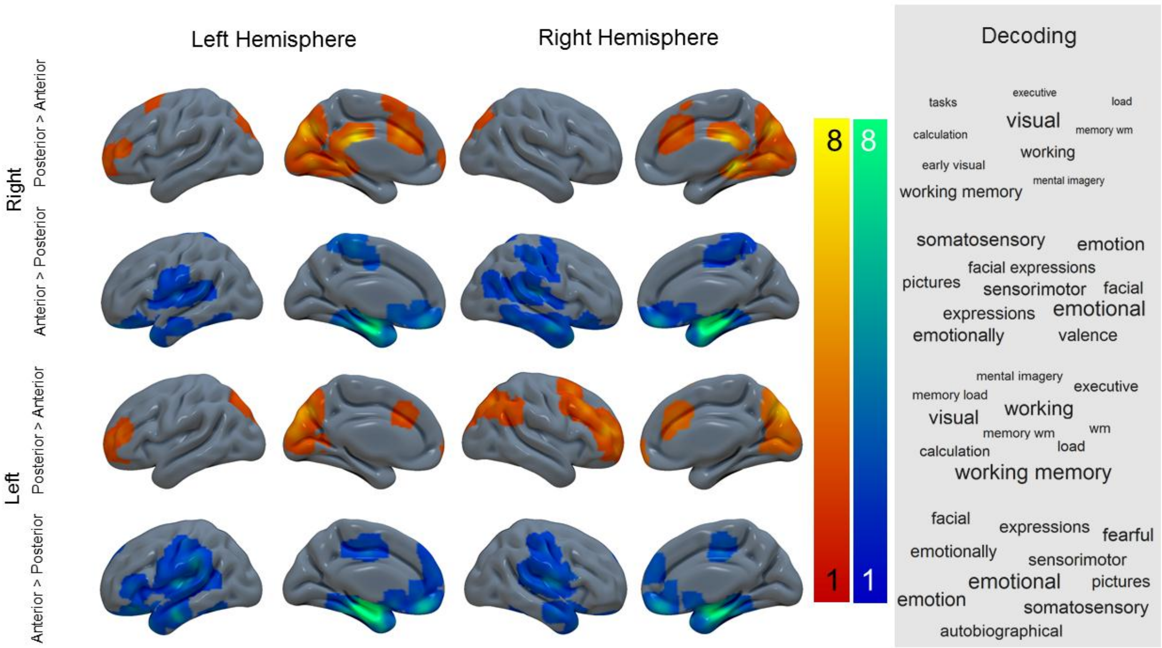


Figure 2. *Differential anterior-posterior connectivity of the hippocampus.* This figure illustrates the regions that show stronger or weaker connectivity with anterior or posterior regions of the hippocampus. Separate maps were calculated for the left and right hemispheres. Regions that show greater connectivity to the anterior hippocampus are indicated in cool colours, while regions showing greater connectivity to the posterior hippocampus are indicated in warm colours. The word clouds on the left hand side of the figure reflect the results of the decoding of the unthresholded maps using Neurosynth. The spatial maps were generated using a cluster forming threshold of Z = 2.6 and corrected for family wise error rate at p < .05.

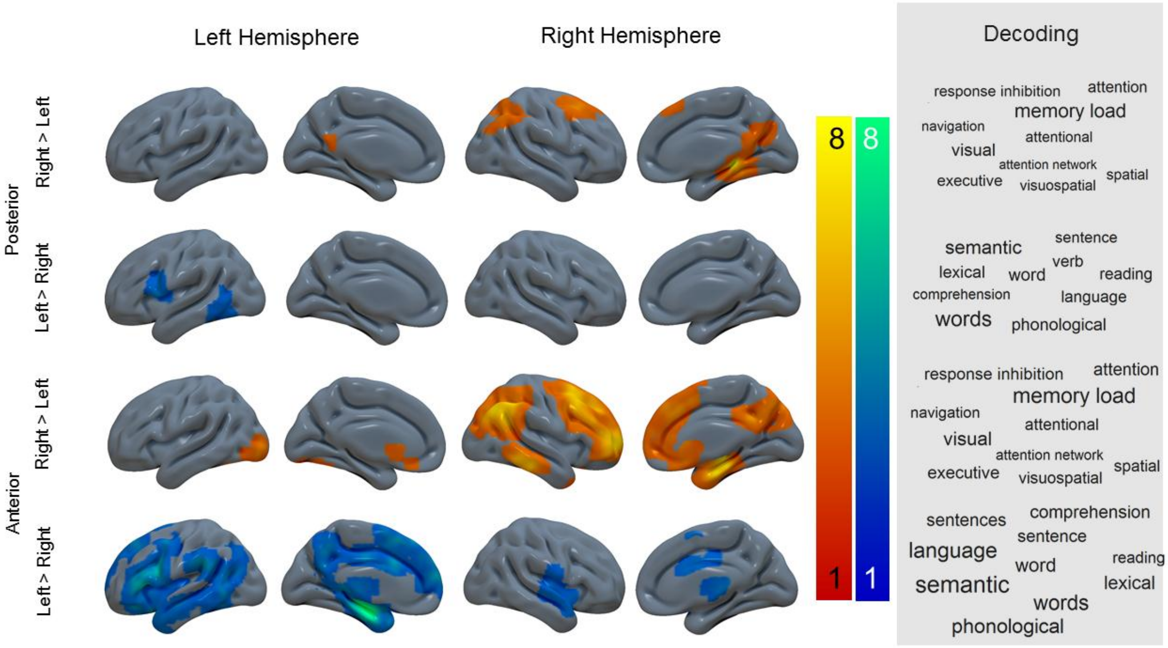


Figure 3. *Differential left-right connectivity of the hippocampus.* This figure illustrates the regions that show greater connectivity with the hippocampus in either the left or right hemisphere. Separate maps were calculated for the anterior and posterior seeds. Regions that show greater connectivity to the hippocampus in the left hemisphere are indicated in cool colours, while regions showing greater connectivity to the hippocampus in the right hemisphere are indicated in warm colours. The word clouds on the left hand side of the figure reflect the results of the decoding of the unthresholded maps using Neurosynth. The spatial maps were generated using a cluster forming threshold of Z = 2.6 and corrected for family wise error rate at $p < .05$.

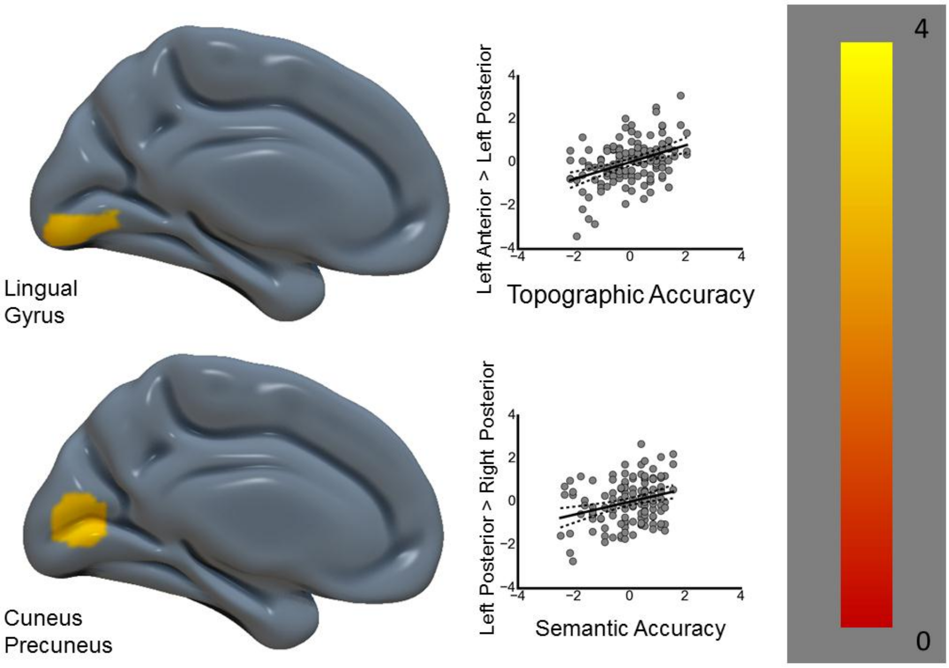


Figure 4. *Cortical regions whose differential connectivity across hippocampal regions discriminated between different types of memory.* This figure illustrates the three regions of cortex (lingual gyrus and cuneus/precuneus) whose pattern of differential connectivity with the hippocampus was predictive of strengths and weaknesses in topographical and semantic memory respectively. Spatial maps were thresholded at Z = 2.6, and corrected for family wise error at p < .0125 to control for the number of comparisons.

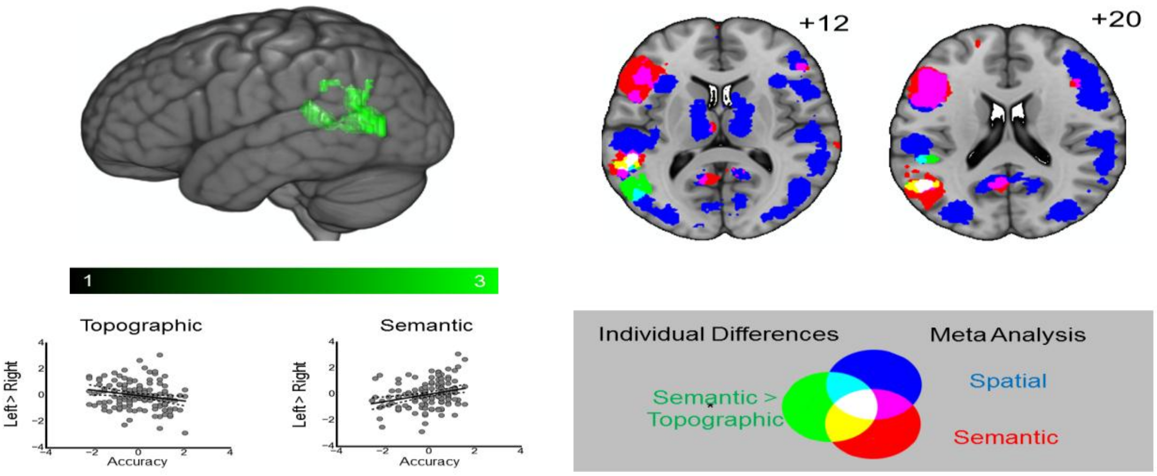


Figure 5. *Double dissociation between hippocampal connectivity to the temporoparietal cortex and the accuracy of semantic and topographic memory.* The left hand panel of this figure

illustrates the contrasting associations between within and between hemisphere hippocampal connectivity and this region of temporoparietal cortex and accuracy at semantic and topographic memory. The right hand panel illustrates the relationship between the spatial extent of this cluster and forward inference meta-analytic maps that describe the term ‘spatial’ and ‘semantic’ generated by Neurosynth. It can be seen that region of cortex that show a double dissociation with respect to different types of memory are common to both spatial maps a pattern that is consistent with a division of labour account of hippocampal contribution to memory.

Conflict of interests
The authors declare no competing financial interests

Acknowledgements

EJ was supported by grants from BBSRC (BB/J006963/1) and the European Research Council (SEMBIND – 283530) and JS was supported by European Research Council (WANDERINGMINDS – 646927). This publication was also made possible through the support of a grant from the John Templeton Foundation, “Prospective Psychology Stage 2: A Research Competition” to Martin Seligman. The opinions expressed in this publication are those of the author(s) and do not necessarily reflect the views of the John Templeton Foundation.

References

Bernasconi, N., Bernasconi, A., Caramanos, Z., Antel, S. B., Andermann, F., & Arnold, D. L. (2003). Mesial temporal damage in temporal lobe epilepsy: A volumetric MRI study of the hippocampus, amygdala and parahippocampal region. *Brain*, *126*(2), 462–469.

Binder, J., Desai, R., Graves, W., & Conant, L. (2009a). Where Is the Semantic System? A Critical Review and Meta-Analysis of 120 Functional Neuroimaging Studies. *Cerebral Cortex*, *19*(12), 2767–2796. Retrieved from papers://3ef1dd7b-eb58-45d1-97b3-39da2cdb02b4/Paper/p492

Binder, J., Desai, R., Graves, W., & Conant, L. (2009b). Where Is the Semantic System? A Critical Review and Meta-Analysis of 120 Functional Neuroimaging Studies. *Cerebral Cortex*, *19*(12), 2767–2796.

Bird, C. M., & Burgess, N. (2008). The hippocampus and memory:insights from spatial processing. *Nature Reviews Neuroscience*, 1–13. Retrieved from papers3://publication/doi/10.1038/nrn2335

Bonnici, H. M., Richter, F. R., Yazar, Y., & Simons, J. S. (2016). Multimodal Feature Integration in the Angular Gyrus during Episodic and Semantic Retrieval. *Journal of Neuroscience*, *36*(20), 5462–5471. Retrieved from http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.4310-15.2016

Braga, R. M., Sharp, D. J., Leeson, C., Wise, R. J. S., & Leech, R. (2013). Echoes of the brain within default mode, association, and heteromodal cortices. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *33*(35), 14031–9. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3810536&tool=pmcentrez&rendertype=abstract

Buzsáki, G., & Moser, E. I. (2013). Memory, navigation and theta rhythm in the hippocampal-entorhinal system. *Nature Neuroscience*, *16*(2), 130–138. Retrieved from http://www.nature.com/doifinder/10.1038/nn.3304%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/23354386

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: an attentional account. *Nature Reviews. Neuroscience*, *9*(8), 613–25. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18641668

Cabeza, R., Mazuz, Y. S., Stokes, J., Kragel, J. E., Woldorff, M. G., Ciaramelli, E., … Moscovitch, M. (2011). Overlapping parietal activity in memory and perception: evidence for the attention to memory model. *Journal of Cognitive Neuroscience*, *23*(11), 3209–17. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21568633

Chase, H. W., Clos, M., Dibble, S., Fox, P., Grace, A. A., Phillips, M. L., & Eickhoff, S. B. (2015). Evidence for an anterior-posterior differentiation in the human hippocampal formation revealed by meta-analytic parcellation of fMRI coordinate maps: Focus on the subiculum. *NeuroImage*, *113*, 44–60.

Collin, S. H. P., Milivojevic, B., & Doeller, C. F. (2015). Memory hierarchies map onto the hippocampal long axis in humans. *Nature Neuroscience*, *18*(11), 1562–1564. Retrieved from http://dx.doi.org/10.1038/nn.4138%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/26479587%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4665212%5Cnhttp://www.nature.com/doifinder/10.1038/nn.4138

Constantinescu, A. O., O'Reilly, J. X., & Behrens, T. E. J. (2016). Organizing conceptual knowledge in humans with a grid-like code. *Science*, *352*, 1464–1468.

Damasio, A. R. (1989). The Brain Binds Entities and Events by Multiregional Activation from Convergence Zones. *Neural Computation*, *1*, 123–132.

Davey, J., Cornelissen, P. L., Thompson, H. E., Sonkusare, S., Hallam, G., Smallwood, J., & Jefferies, E. (2015a). Automatic and Controlled Semantic Retrieval: TMS Reveals Distinct Contributions of Posterior Middle Temporal Gyrus and Angular Gyrus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *35*(46), 15230–9. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4649000&tool=pmcentrez&rendertype=abstract

Davey, J., Cornelissen, P. L., Thompson, H. E., Sonkusare, S., Hallam, G., Smallwood, J., & Jefferies, E. (2015b). Automatic and Controlled Semantic Retrieval: TMS Reveals Distinct

Contributions of Posterior Middle Temporal Gyrus and Angular Gyrus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *35*(46), 15230–9.

Davey, J., Thompson, H. E., Hallam, G., Karapanagiotidis, T., Murphy, C., De Caso, I., … Jefferies, E. (2016). Exploring the role of the posterior middle temporal gyrus in semantic cognition: Integration of anterior temporal lobe with goal-oriented cognition. *NeuroImage*. Retrieved from http://linkinghub.elsevier.com/retrieve/pii/S1053811916301719

Dusek, J. A., & Eichenbaum, H. (1997). The hippocampus and memory for orderly stimulus relations. *Proceedings of the National Academy of Sciences of the United States of America*, *94*(13), 7109–14. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=21293&tool=pmcentrez&rendertype=abstract

Duvernoy, H. (1988). *The Human Hippocampus*. *An Atlas of Applied Anatomy*. J.F. Bergmann-Verlag.

Eichenbaum, H., & Cohen, N. J. (2004). *From Conditioning to Conscious Recollection: Memory systems of the brain*. *From Conditioning to Conscious Recollection: Memory systems of the brain*. Oxford University Press USA.

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences*, 201602413. Retrieved from http://www.pnas.org/lookup/doi/10.1073/pnas.1602413113

Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends in Cognitive Sciences*, *12*(10), 388–396.

Fox, K. C. R., Spreng, R. N., Ellamil, M., Andrews-Hanna, J. R., & Christoff, K. (2016). Corrigendum to “The wandering brain: Meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes” [NeuroImage 111 (2015) 611-621]. *NeuroImage*, *111*, 611–621. Retrieved from http://dx.doi.org/10.1016/j.neuroimage.2015.02.039

Greenberg, D. L., & Verfaellie, M. (2010). Interdependence of episodic and semantic memory: evidence from neuropsychology. *J Int Neuropsychol Soc*, *16*(5), 748–753. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20561378

Harness, A., Jacot, L., Scherf, S., White, A., & Warnick, J. E. (2008). Sex differences in working memory. *Psychological Reports*, *103*(1), 214–218.

Hartley, T., Bird, C. M., Chan, D., Cipolotti, L., Husain, M., Varga-Khadem, F., & Burgess, N. (2007). The hippocampus is required for short-term topographical memory in humans. *Hippocampus*, *17*(1), 34–38.

Hassabis, D., & Maguire, E. A. (2011). The Construction System of the Brain. *Predictions in the Brain: Using Our Past to Generate a Future*.

Hill, A. C., Laird, A. R., & Robinson, J. L. (2014). Gender differences in working memory networks: A BrainMap meta-analysis. *Biological Psychology*, *102*, 18–29.

Horner, A. J., Bisby, J. A., Bush, D., Lin, W.-J., & Burgess, N. (2015). Evidence for holistic episodic recollection via hippocampal pattern completion. *Nature Communications*, *6*, 7462. Retrieved from http://www.nature.com/ncomms/2015/150702/ncomms8462/full/ncomms8462.html

Humphreys, G. F., & Lambon Ralph, M. A. (2014). Fusion and Fission of Cognitive Functions in the Human Parietal Cortex. *Cerebral Cortex*. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/25205661

Jefferies, E. (2013). The neural basis of semantic cognition: Converging evidence from neuropsychology, neuroimaging and TMS. *Cortex*, *49*(3), 611–625.

Krieger-Redwood, K. M. (2012). *An Investigation of Phonological and Semantic Control Using TMS and fMRI*.

Kuhl, B. A., & Chun, M. M. (2014). Successful remembering elicits event-specific activity patterns in lateral parietal cortex. *J Neurosci*, *34*(23), 8051–8060. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/24899726

Kulaga-Yoskovitz, J., Bernhardt, B. C., Hong, S.-J. J., Mansi, T., Liang, K. E., van der Kouwe, A. J. W., … Bernasconi, N. (2015). Multi-contrast submillimetric 3 Tesla hippocampal subfield segmentation protocol and dataset. *Scientific Data*, *2*, 150059. Retrieved from http://www.nature.com/articles/sdata201559

Manns, J. R., Hopkins, R. O., & Squire, L. R. (2003). Semantic memory and the human hippocampus. *Neuron*, *38*(1), 127–133.

Marr, D. (1971). Simple Memory: A Theory of Archicortex. *Philos Trans R Soc Lond B Biol Sci.*, *262*, 23–81.

Medea, B., Karapanagiotidis, T., Konishi, M., Ottaviani, C., Margulies, D., Bernasconi, A., … Smallwood, J. (2016). How do we decide what to do? Resting-state connectivity patterns and components of self-generated thought linked to the development of more concrete personal goals. *Experimental Brain Research*. Retrieved from http://link.springer.com/10.1007/s00221-016-4729-y

Mesulam, M. M. (1981). A cortical network for directed attention and unilateral neglect. *Annals of Neurology*, *10*(4), 309–325.

Moscovitch, M., Cabeza, R., Winocur, G., & Nadel, L. (2016). Episodic memory and beyond: The hippocampus and neocortex in transformation. *Annual Review of Psychology*, *67*(1), 105–134. Retrieved from http://www.annualreviews.org/doi/10.1146/annurev-psych-113011-143733

Murphy, K., Birn, R. M., Handwerker, D. A., Jones, T. B., & Bandettini, P. A. (2009). The impact of global signal regression on resting state correlations: Are anti-correlated networks introduced? *NeuroImage*, *44*(3), 893–905.

Nadel, L., & Peterson, M. A. (2013). The hippocampus: part of an interactive posterior representational system spanning perceptual and memorial systems. *Journal of Experimental Psychology. General*, *142*(4), 1242–54. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23895347

Nelson, D. L., McEvoy, C. L., & Schreiber, T. a. (2004). The University of South Florida free association, rhyme, and word fragment norms. *Behavior Research Methods, Instruments, & Computers*, *36*(3), 402–407.

Noonan, K. A., Jefferies, E., Visser, M., & Lambon Ralph, M. A. (2013). Going beyond inferior prefrontal involvement in semantic control: evidence for the additional contribution of dorsal angular gyrus and posterior middle temporal cortex. *Journal of Cognitive Neuroscience*, *25*(11), 1824–50. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23859646

Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know?: The representation of semantic knowledge in the human brain. *Nature Reviews*, *8*(12), 976–987. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18026167

Payne, J. D., Tucker, M. A., Ellenbogen, J. M., Wamsley, E. J., Walker, M. P., Schacter, D. L., & Stickgold, R. (2012). Memory for semantically related and unrelated declarative information: The benefit of sleep, the cost of wake. *PLoS ONE*, *7*(3), 1–7.

Peelen, M. V, & Caramazza, a. (2012). Conceptual Object Representations in Human Anterior Temporal Cortex. *Journal of Neuroscience*, *32*(45), 15728–15736. Retrieved from http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.1953-12.2012

Poppenk, J., Evensmoen, H. R., Moscovitch, M., & Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends in Cognitive Sciences*, *17*(5), 230–240.

Power, J. D., Mitra, A., Laumann, T. O., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2014). Methods to detect, characterize, and remove motion artifact in resting state fMRI. *NeuroImage*, *84*, 320–341.

Ranganath, C., & Ritchey, M. (2012). Two cortical systems for memory-guided behaviour. *Nature Reviews Neuroscience*, *13*(10), 713–726. Retrieved from http://dx.doi.org/10.1038/nrn3338

Rice, G. E., Ralph, M. A. L., & Hoffman, P. (2015). The roles of left versus right anterior temporal lobes in conceptual knowledge: An ALE meta-analysis of 97 functional neuroimaging studies. *Cerebral Cortex*, *25*(11), 4374–4391.

Ritchey, M., Montchal, M. E., Yonelinas, A. P., & Ranganath, C. (2015). Delay-dependent contributions of medial temporal lobe regions to episodic memory retrieval. *eLife*, *4*.

Robinson, J. L., Salibi, N., & Deshpande, G. (2016). Functional connectivity of the left and right hippocampus: Evidence for functional lateralization using meta-analytic approaches and ultra-high field functional neuroimaging. *NeuroImage*, *135*, 64–78. Retrieved from http://dx.doi.org/10.1016/j.neuroimage.2016.04.022

Rosenbaum, R. S., Köhler, S., Schacter, D. L., Moscovitch, M., Westmacott, R., Black, S. E., … Tulving, E. (2005). The case of K.C.: Contributions of a memory-impaired person to memory theory. *Neuropsychologia*, *43*(7), 989–1021.

Rugg, M. D., & Vilberg, K. L. (2013). Brain networks underlying episodic memory retrieval. *Current Opinion in Neurobiology*, *23*(Box 1), 255–260.

Ryan, L., Cox, C., Hayes, S. M., & Nadel, L. (2008). Hippocampal activation during episodic and semantic memory retrieval: Comparing category production and category cued recall. *Neuropsychologia*, *46*(8), 2109–2121.

Saxe, R., & Kanwisher, N. (2003). People thinking about thinking people: The role of the temporo-parietal junction in “theory of mind.” *NeuroImage*, *19*(4), 1835–1842.

Schacter, D. L., Addis, D. R., & Buckner, R. L. (2007). Remembering the past to imagine the future: the prospective brain. *Nature Reviews Neuroscience*, *8*(9), 657–661. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/17700624

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *20*, 11–21.

Seghier, M. (2012). The Angular Gyrus: Multiple Functions and Multiple Subdivisions. *The Neuroscientist*, *19*(1), 43–61. Retrieved from http://discovery.ucl.ac.uk/1347412/

Sheldon, S., Farb, N., Palombo, D. J., & Levine, B. (2016). Intrinsic medial temporal lobe connectivity relates to individual differences in episodic autobiographical remembering. *Cortex*, *74*, 206–216.

Spiers, H. J., Maguire, E. A., & Burgess, N. (2001). Hippocampal Amnesia. *Neurocase : Case Studies in Neuropsychology, Neuropsychiatry, and Behavioural Neurology*, *7*(5), 357–382.

Spreng, R. N., Mar, R. A., & Kim, A. S. N. (2008). The Common Neural Basis of Autobiographical Memory, Prospection, Navigation, Theory of Mind, and the Default Mode: A Quantitative Meta-analysis. *Journal of Cognitive Neuroscience*, *21*(3), 489–510. Retrieved from http://dx.doi.org/10.1162/jocn.2008.21029%5Cnhttp://www.mitpressjournals.org/doi/a bs/10.1162/jocn.2008.21029?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub=pubmed%5Cnhttp://www.mitpressjournals.org/doi/pdf/10.1162/jocn.2008.21029?url_ver=Z39.8

Strange, B. A., Witter, M. P., Lein, E. S., & Moser, E. I. (2014). Functional organization of the hippocampal longitudinal axis. *Nature Publishing Group*, *15*(10), 655–669. Retrieved from http://www.scopus.com/inward/record.url?eid=2-s2.0-84908654563&partnerID=40&md5=faf1a91ddf30b74ebd329fa9d136f1ec%5Cnhttp://www.nature.com/nrn/journal/v15/n10/pdf/nrn3785.pdf

Teyler, T. J., & Rudy, J. W. (2007). The hippocampal indexing theory and episodic memory: Updating the index. *Hippocampus*, *17*(12), 1158–1169.

Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connely, A., Van Paeschen, W., & Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory. *Science PG - 376*, *277*, 380.

Vigneau, M., Beaucousin, V., Herve, P. Y., Duffau, H., Crivello, F., Houde, O., … Tzourio-Mazoyer, N. (2006). Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *NeuroImage*, *30*(4), 1414–1432.

Wagner, I. C., van Buuren, M., Bovy, L., & Fernández, G. (2016). Parallel Engagement of Regions Associated with Encoding and Later Retrieval Forms Durable Memories. *Journal of Neuroscience*, *36*(30), 7985–7995. Retrieved from http://www.jneurosci.org/cgi/doi/10.1523/JNEUROSCI.0830-16.2016

Wagner, I. C., van Buuren, M., Kroes, M. C. W., Gutteling, T. P., van der Linden, M., Morris, R. G., & Fernández, G. (2015). Schematic memory components converge within angular gyrus during retrieval. *eLife*, *4*(NOVEMBER2015).

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods*, *8*(8), 665–670. Retrieved from papers://fd97edd0-de1d-401e-87f3-202830b99eeb/Paper/p14347

Zeidman, P., & Maguire, E. A. (2016). Anterior hippocampus: the anatomy of perception, imagination and episodic memory. *Nature Reviews Neuroscience*, *17*(3), 173–182. Retrieved from http://dx.doi.org/10.1038/nrn.2015.24

Highlights

- Anatomical segments of hippocampus (HC) have unique functional connectivity profiles.
- It is hypothesised that these reflect a role for HC in episodic, semantic and topographic memory.
- We tested the relation between HC connectivity and variation in different memory abilities.

- Anterior HC connectivity to temporo-parietal cortex dissociated semantic and topographic memory
- Our findings suggest a division of labour in HC contribution to different types of memory

Supplementary Materials

Supplementary table 1: mean z scored accuracy for Topographic (4MT), Semantic (RJT) and Episodic (PAT) memory tasks for each participant within the current study. Each memory task was used as a regressor of interest within the study to predict resting state connectivity. An analysis of covariance showed low collinearity between regressor of interest, Variance Inflation Factors (VIF) were extremely low for each predictor variable (4MT and RJT VIF = 1.11, 4MT and PAT VIF = 1, RJT and PAT VIF = 1).

Participant	4MT score	RJT score	PAT score
1	0.07	-1.31	0.65
2	-0.37	-0.16	-1.49
3	-0.59	0.56	1.64
4	0.07	0.85	0.78
5	0.07	-0.16	0.87
6	0.50	0.42	0.78
7	-1.25	-0.16	-1.79
8	-1.25	-1.31	-0.08
9	-1.03	0.42	0.01
10	-2.13	-0.16	-0.08
11	0.73	-1.31	0.78
12	1.16	0.85	0.87
13	0.07	0.42	1.64
14	1.16	-0.16	0.14
15	-0.15	0.42	1.43
16	-0.15	0.13	-0.85
17	0.94	1.28	1.08
18	-0.59	0.85	-1.15
19	0.50	0.13	1.21
20	-0.37	-0.16	1.64
21	-0.59	1.14	-2.35
22	0.94	0.85	-0.94
23	0.94	1.28	-0.42
24	0.29	0.13	0.78
25	0.50	0.56	-0.85
26	-0.37	-1.31	-1.71
27	-1.25	-2.47	-0.94

28	-0.15	0.56	0.65
29	0.07	-1.74	0.44
30	-0.81	0.85	0.14
31	-0.15	-0.30	-0.08
32	-1.90	-0.88	0.78
33	-1.90	0.85	-0.20
34	-1.03	-0.59	-0.08
35	0.07	1.57	-1.36
36	1.60	-2.13	0.44
37	1.16	0.42	-1.15
38	0.50	0.85	1.00
39	-0.37	-2.32	0.14
40	-0.37	1.57	-0.85
41	-1.47	-1.74	0.78
42	-0.59	0.13	1.00
43	0.07	1.14	0.44
44	1.39	0.56	-0.72
45	-0.37	0.42	1.00
46	-0.59	0.85	0.01
47	0.73	0.42	0.44
48	-0.37	1.14	1.00
49	1.82	0.56	-0.72
50	-1.69	0.13	-0.08
51	0.73	-0.88	-0.29
52	0.94	-0.16	0.35
53	0.94	-0.59	1.08
54	0.29	1.14	-0.94
55	2.04	-0.30	-0.94
56	-0.37	-0.16	-0.72
57	1.16	1.14	-1.06
58	0.07	0.56	-1.15
59	-0.37	-2.13	-0.51
60	-0.59	0.42	-1.49
61	0.94	0.56	1.08
62	-0.81	0.13	0.65
63	-1.47	0.42	-1.36
64	-2.13	-2.13	-1.92
65	0.07	-0.88	0.78
66	-1.47	0.56	-0.94
67	0.50	0.13	-0.63
68	1.16	0.13	-1.92
69	2.04	1.14	0.44
70	-0.37	-0.59	-1.92
71	-0.37	-0.30	-0.20
72	-1.03	-0.30	1.00
73	0.94	0.56	-1.49
74	-1.47	-2.03	-0.94

75	-1.69	0.85	-0.08
76	0.94	0.13	0.22
77	1.16	1.28	1.00
78	0.73	1.14	1.51
79	1.82	0.56	-1.06
80	1.39	0.85	-0.29
81	0.07	-0.16	0.14
82	0.29	-0.16	0.87
83	-0.81	-2.32	-2.01
84	-0.81	-0.88	0.14
85	1.39	0.85	0.44
86	0.29	1.14	0.35
87	-1.03	-2.03	-0.42
88	1.16	0.42	-2.01
89	1.16	0.56	0.65
90	-0.59	0.56	-0.42
91	1.39	-0.16	1.51
92	2.04	-0.16	0.35
93	0.73	1.14	-1.15
94	-0.15	-1.02	1.00
95	0.94	0.56	-2.22
96	1.39	-0.30	-0.20
97	-0.15	-0.30	-0.72
98	1.39	-0.16	-2.22
99	-0.81	-0.16	-1.06
100	-0.59	-1.02	0.57
101	-0.37	0.56	-0.20
102	0.50	0.13	-1.15
103	-1.47	-0.59	0.35
104	-0.59	-0.16	0.01
105	-1.69	-0.59	-0.08
106	-0.81	-1.31	0.78
107	0.94	-2.03	0.78
108	-0.59	-0.16	-1.06
109	-1.03	0.85	1.08
110	-0.81	-1.31	0.35
111	0.29	0.56	-1.49
112	-0.81	1.28	-0.51
113	-1.69	-1.60	-0.08
114	1.16	0.13	0.57
115	-0.15	1.14	1.30
116	-2.13	-1.60	1.08
117	0.07	1.57	1.00
118	-1.47	-1.31	-1.15
119	0.07	0.56	0.44
120	-2.13	-0.59	0.01
121	-0.37	0.56	0.35

122	0.73	-0.88	-0.29
123	-0.59	0.56	1.21
124	1.60	0.85	0.78
125	0.29	-0.59	0.57
126	0.51	1.14	0.78
127	-1.03	1.14	1.08
128	-1.69	-1.31	1.30
129	-0.15	0.56	0.65
130	0.29	0.56	-0.94
131	0.73	0.42	0.65
132	1.16	-0.59	1.00
133	1.38	0.42	1.08
134	0.29	1.28	0.87
135	0.51	0.85	1.64
136	0.73	-0.30	0.65