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

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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 connectivity between the intracalcarine/cuneus 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.

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 and Milner, 1957; Spiers et al., 2001) and neuroimaging investigations highlight the hippocampus as important in recollection (for a review see Rugg and 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 and Moser (2013)). The hippocampus and the medial temporal lobe work in tandem, forming

semantic relationships based on associative learning (Manns et al., 2003; Ryan et al., 2008; Greenberg and Verfaellie, 2010; Constantinescu et al., 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 et al. (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 et al., 2015). It is increasingly recognised that differences in connectivity along the posterior-anterior axis of the hippocampus could give rise to functional specialisation

(Poppenk et al., 2013; Strange et al., 2014; Ranganath and 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 and Peterson, 2013; Bird and Burgess, 2008; Hassabis and 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 et al., 2007; Jefferies, 2013; Rice et al., 2015; Peelen and 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 et al., 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 et al., 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-h 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 min 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 Fig. 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 and 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 3 s. 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 min 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 min 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.