

OPINION

Anterior hippocampus: the anatomy of perception, imagination and episodic memory

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Abstract | The brain creates a model of the world around us. We can use this representation to perceive and comprehend what we see at any given moment, but also to vividly re-experience scenes from our past and imagine future (or even fanciful) scenarios. Recent work has shown that these cognitive functions — perception, imagination and recall of scenes and events — all engage the anterior hippocampus. In this Opinion article, we capitalize on new findings from functional neuroimaging to propose a model that links high-level cognitive functions to specific structures within the anterior hippocampus.

The hippocampus is critical for learning, memory and cognition. It is one of the most studied brain structures in neuroscience, and efforts to understand its functions continue apace. In particular, there is considerable interest in functional differences between neural populations located at different points along its anterior–posterior axis^{1–5}. A recent literature review³ showed that, in addition to the gradients of gene expression and connectivity that vary along the length of the hippocampus, the anterior portion of the hippocampus (also known as the head, ventral or temporal region) can be distinguished from the intermediate and posterior sections (also known as the tail, dorsal or septal regions) by sharp changes in these functional characteristics.

Owing to its complex anatomy, the anterior hippocampus (particularly that of humans) has proved to be difficult to study⁶. It has an intricate structure with unique cellular morphology and is positioned at the junction between the parahippocampal gyrus, the amygdala and the posterior hippocampus. It has widespread connectivity, and hippocampal lesions that include damage to the anterior hippocampus have a deleterious effect on learning, memory and navigation^{7–9}.

However, we are only beginning to understand the precise anatomy of this brain region in humans¹⁰, and consequently little is known about the specific structures within the anterior hippocampus that contribute to these important cognitive functions.

In this article, we focus on the human anterior hippocampus. We summarize current knowledge of its anatomy and highlight a striking consistency in the functional MRI (fMRI) literature, which suggests that specific substructures within the anterior hippocampus make critical contributions to episodic memory, imagination and visual scene perception. Claims that the hippocampus (and the medial temporal lobes more generally) performs functions beyond memory (such as visual perception) are heavily contested¹¹, particularly because it is difficult to design experiments that unequivocally control for memory encoding and retrieval. We propose a model of anterior hippocampal function that takes into account the importance of anatomical detail and refers to known connectivity across species; this model may help to clarify recent discussions of functional differences in the long axis of the hippocampus^{1–4} as well as the relationship between visual perception and memory.

Anterior hippocampus anatomy

In humans, the hippocampus is cradled by the parahippocampal gyrus, which is positioned beneath it. The anterior part of the parahippocampal gyrus bends over and rests upon itself, forming the uncus. The various gyri that are visible on the surface of the brain (BOX 1) cover both the amygdala and the anterior portion of the hippocampus. Beneath this surface, the hippocampus is divided into cytoarchitecturally defined subfields. These are commonly thought of as being arranged in a canonical circuit, which can be visualized in the cross-section of the main body of the hippocampus (FIG. 1). In this circuit, neurons in the entorhinal cortex (EC), which is part of the neighbouring parahippocampal gyrus, project to the dentate gyrus (DG), which in turn drives subfield CA3 then CA2, CA1 and the subiculum. The subiculum and CA1 then project back to the EC. Also visible in this plane are regions related to, but distinct from, the subiculum: the prosubiculum, the presubiculum and the parasubiculum. The prosubiculum is situated between CA1 and the subiculum. However, despite many differences between its connectivity and that of the subiculum¹², these two regions are not normally separated in human neuroimaging because their borders are not visible with MRI. The presubiculum and the parasubiculum are situated between the subiculum and the EC. These regions can be delineated with high-resolution MRI¹⁰, which offers new opportunities to study their functions in humans.

Understanding the arrangement of the subfields in the anterior hippocampus requires awareness of their three-dimensional shape. The main body of the hippocampus bends medially in its anterior portion (FIG. 1a) to form the extraventricular part of the anterior hippocampus, which is positioned within the uncus. As a result, CA1 and the subiculum must bend around a wider radius than the other subfields¹³. Thus, the most anterior portion of the hippocampus is dominated by CA1 and the subiculum (FIG. 1b), whereas the more posterior part of the uncus contains only the DG, CA2 and CA3 (FIG. 1d). After the

medial turn within the uncus, the subfields bend upwards, ascending vertically towards the amygdala (FIG. 1b,c), which changes their orientation from the coronal to the axial plane.

Subfields within the uncus have cellular ‘peculiarities’ (REF. 14): for example, CA1 in the uncus — referred to as CA1’ — has smaller and more densely packed neurons than CA1 in the body of the hippocampus¹³ (note that CA1’ is labelled uncal subiculum in an alternative nomenclature¹⁵). The vertical part of the uncus has particularly differentiated cytoarchitecture — for instance, vertical CA1’ contains more densely packed pyramidal cell bodies than horizontal CA1’ or CA1 of the hippocampal body¹⁰. The functional implications of these cellular differences are unknown.

Although the subfields are usually studied in slices perpendicular to the hippocampal long axis (the coronal plane in humans; see FIG. 1b–e), connections also extend through the length of the hippocampus^{16,17}. In the coronal plane and with a slight anterior inclination,

mossy fibres project from the DG to CA3, and upon reaching distal CA3 they change direction to extend 3–5 mm in the anterior direction¹⁷. By contrast, associational and local connections within the DG — which may have excitatory and inhibitory roles, respectively¹⁶ — extend bidirectionally along much of the length of the hippocampus. The DG in the uncus is connected to the anterior DG in the main body of the hippocampus through these associational projections¹⁶. The connection from CA3 to CA1 (the Schaffer collaterals) and connections within CA3 also have longitudinal projections through most of the hippocampus¹⁷. Once again, the uncus is distinct, with the targets of projections of the uncal CA3 (CA3’) being largely confined to CA3’ and CA1’. The human hippocampus can therefore be divided into subfields in the main body of the hippocampus that are connected in cross-section and longitudinally, as well as modified subfields that comprise the uncus and have more limited connectivity with the anterior hippocampus.

Importantly, there are differences in the hippocampal anatomy of different species. The uncus is particularly highly developed in primates, and the degree to which it is homologous to its counterpart in rodents is uncertain^{10,13}. There are also differences in connectivity. Whereas rodents have commissural connections along the length of the hippocampus, in monkeys these connections are largely restricted to anterior regions, particularly the uncus¹⁸. In monkeys, cells in the DG of the uncus project via the white matter of the fimbria or fornix, before crossing hemispheres via the ventral hippocampal commissure¹⁹, returning along the same pathway in the opposite hemisphere to terminate in the contralateral uncus. Other regions associated with the hippocampus — the presubiculum, the EC and the posterior parahippocampal cortex — connect across hemispheres via the dorsal hippocampal commissure. These findings point to a striking role for the anterior hippocampus in connecting the hippocampi of each hemisphere. It has been suggested that

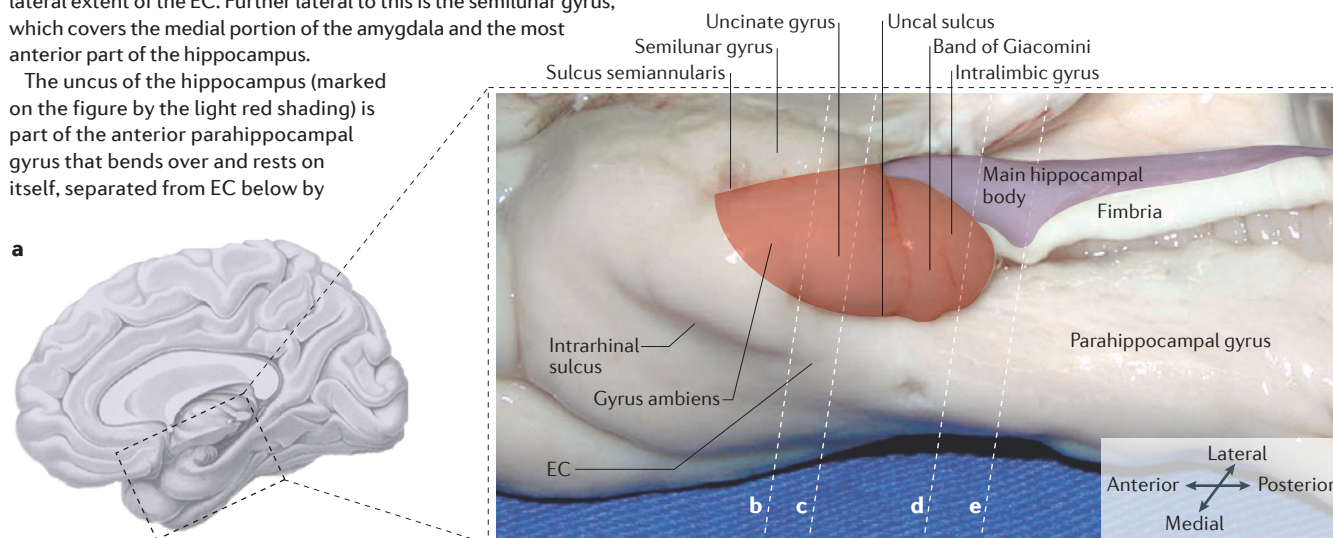
Box 1 | A tour of the anterior hippocampus

The anterior hippocampus may be understood in terms of its cytoarchitecture (see the main text) or in terms of the features that are visible on the surface of the brain, which are summarized here based on previous observations^{10,13,94}. See part **a** of the figure for context. Dashed lines labelled **b–e** correspond to the coronal slices shown in FIG. 1.

Starting in the parahippocampal gyrus and moving anteriorly (towards the left of the figure), the gyrus becomes the entorhinal cortex (EC). Its approximate position is indicated for clarity, although its borders are not visible on the brain’s surface (in coronal slices, the EC appears approximately at the level of the lateral geniculate nucleus¹⁰¹). The parahippocampal gyrus then bends upwards, separated by the narrow intrarhinal sulcus from the gyrus ambiens above. The gyrus ambiens extends laterally to the sulcus semiannularis, which marks the lateral extent of the EC. Further lateral to this is the semilunar gyrus, which covers the medial portion of the amygdala and the most anterior part of the hippocampus.

The uncus of the hippocampus (marked on the figure by the light red shading) is part of the anterior parahippocampal gyrus that bends over and rests on itself, separated from EC below by

the uncal sulcus. Moving posteriorly along the uncus (towards the right of the figure), the gyrus ambiens becomes the uncinat gyrus, which contains the hippocampal–amygdaloid transition area (HATA) (FIG. 1b,c). Next, the uncus becomes the band of Giacomini and finally the intralimbic gyrus, getting progressively smaller towards the posterior. The point at which the intralimbic gyrus is no longer visible in coronal section is a landmark for the posterior-most slice of the anterior hippocampus². Thus, the anterior part of the uncus comprises the uncinat gyrus, whereas the posterior consists of the band of Giacomini and the intralimbic gyrus. The main hippocampal body and fimbria are positioned lateral to the uncus. Part **a** is adapted with permission from REF. 102, Springer. Photograph of the dissected brain is adapted from REF. 103.



the ventral hippocampal commissure may not exist in humans²⁰; however, there is a notable lack of research relating human hippocampal connectivity to that of non-human primates.

Representing the environment

We can vividly re-experience past events, simulate future events and imagine fictitious scenarios, in addition to experiencing the environment we currently inhabit. To achieve this, we must be able to construct internal representations of environments on the basis of incoming sensory information and/or prior experience. As we argue, there is evidence that structures within the medial part of the anterior hippocampus have a role in constructing these representations.

Decades of research, carried out primarily in rodents, has revealed several key cell types in the hippocampus and neighbouring structures that contribute to spatial processing. Place cells in CA1 represent an animal's location²¹, whereas grid cells in the EC, presubiculum and parasubiculum may provide a metric-like framework for spatial representation^{22,23}. Head direction cells, which represent the animal's heading relative to fixed landmarks, have been discovered in several interconnected regions including the presubiculum, postsubiculum, anterodorsal thalamus, EC, retrosplenial cortex, mammillary bodies and thalamus^{23–25}. More recently, boundary vector (border) cells, which represent the position of environmental boundaries, have been found in the subiculum, presubiculum, parasubiculum and EC²⁶. In humans, fMRI and neuropsychological studies have suggested that the hippocampus^{9,27,28}, EC²⁹ and retrosplenial cortex³⁰ are implicated in spatial navigation.

The properties of place cells are modulated by their anterior–posterior position within the hippocampus. In rodents, the firing fields of ventral (anterior in humans) place cells are larger than those of dorsal (posterior in humans) place cells³¹. The notion that the anterior hippocampus represents less specific information contributed to the proposal² that anterior–posterior differences in the hippocampus can be understood as a gradient in the level of detail, from coarse representations in the anterior hippocampus to fine detail in the posterior. An alternative explanation comes from a recent finding³² that an animal's precise location can be decoded from the activity of cell populations in

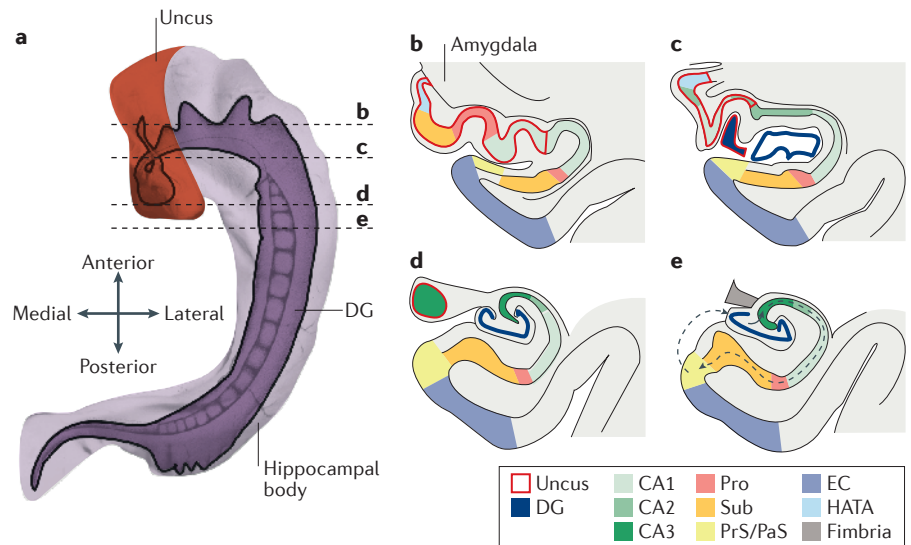


Figure 1 | Anatomy of the anterior hippocampus. **a** | A schematic showing a dorsal view of the hippocampus with the dentate gyrus (DG) visible inside. The main hippocampus body as well as the uncus are indicated. **b–e** | Coronal slices showing the hippocampal subfields in the anterior hippocampus. Red lines indicate subfields that are found within the uncus and which have distinct cyto-architectural properties relative to the main body of the hippocampus. The slices in panels **b** and **c** are at the level of the uncinate gyrus, whereas the slice in panel **d** is at the level of the intralimbic gyrus. The arrows in panel **e** indicate the flow of information in the canonical hippocampal circuit in the body of the hippocampus. EC, entorhinal cortex; HATA, hippocampal–amygdaloid transition area; Pro, pro-subiculum; PrS/PaS, presubiculum and parasubiculum. Panel **a** is adapted with permission from REF. 94, Springer. Panels **b–e** are adapted with permission from REF. 10, Wiley.

the anterior hippocampus, despite each individual cell only representing a larger area of the environment. Computer simulations demonstrated that this distributed representation in the anterior hippocampus (which is no less precise than that of the posterior hippocampus) makes it better suited to generalizing across environments (pattern completion), whereas the smaller place fields in the posterior hippocampus would be better at resisting interference from similar locations (pattern separation³³). Although this finding is still to be replicated, the general consensus is that having a spatially large-scale or generalizable representation of the environment depends on the anterior hippocampus^{2,32}.

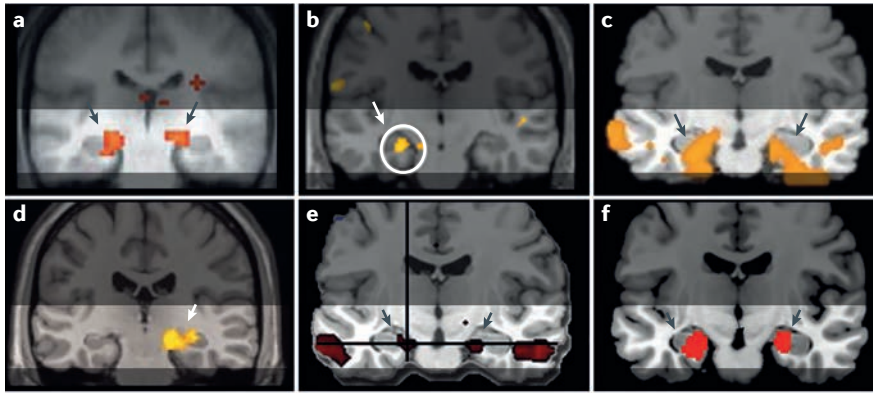
Hippocampal cell populations involved in spatial processing represent both the current state of the animal and also imagined future locations^{34–36}, and enable ‘replay’ of remembered past locations³⁷. However, recent evidence suggests that a purely spatial account of hippocampal function is insufficient. For example, some aspects of allocentric spatial navigation are preserved in patients with bilateral hippocampal damage^{9,38}, whereas these individuals exhibit a clear deficit in imagining scenes^{39,40}.

Recalling and imagining scenes

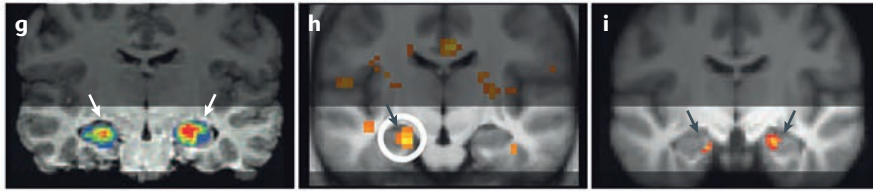
Scenes are coherent object-containing spaces within which we can potentially operate. If scenes develop over time, they may be referred to as events or episodes (however, a temporal dimension is not required in order to involve the hippocampus^{39,41}). Tasks that require scenes or events to be imagined or recalled^{41–50}, including those that involve navigation²⁸, engage the hippocampus, and performance in these tasks is impaired or abolished following bilateral hippocampal lesions^{7–9}.

It has been hypothesized that the hippocampus contributes to performance in these tasks by providing a spatial representation (or model) of the scene being processed^{51,52}. If so, common subregions within the hippocampus should be engaged by any task that involves the construction of scene representations. Indeed, as described below, there is a striking consistency in the fMRI results across many studies in the literature, which differed in the tasks that were used but all involved naturalistic scenes. These studies reported activation of the anterior hippocampus, and close examination of their findings reveals a common region of activation in the medial bank of the anterior hippocampus, which we refer to as amHipp (FIG. 2a–j). Here, we

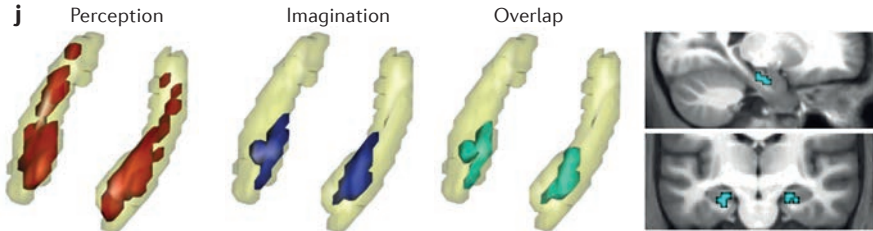
Imagination and recall of scenes and/or events



Perception of scenes and/or events



Perception and imagination of scenes



use a working definition of the anterior hippocampus as the region having an MNI y coordinate of less than or equal to -22 (ensuring complete coverage of the uncus), and we define amHipp functionally as clusters of activated locations (voxels) that peak in the anterior hippocampus and exhibit a clear bias towards the medial half of the structure. Using this definition, it can be seen that many cognitive tasks engage amHipp (see below). Although several of these tasks, particularly those involving visual stimuli, also engage other parts of the hippocampus, amHipp appears to be the most consistently engaged subregion across studies and often shows the greatest effect size. Quantifying the proportion of studies that have found this specific region to be engaged during recall and imagination would require a formal meta-analysis, which would be complicated by the limited scanning resolution of some studies. However, our observation is that this finding is the norm rather than the exception. As we discuss below, high-resolution MRI is starting to relate this fMRI activity to the precise underlying anatomy.

Episodic memory and imagination.

fMRI studies of episodic (autobiographical) memory, which require participants to vividly recall specific events from their past, generally find that a 'core network' of brain regions — including the anterior hippocampus — is engaged^{53,54} (BOX 2). Activation within the hippocampus may be limited to amHipp. For example, when subjects were cued to imagine static atemporal scenes based on short descriptions, amHipp was the only part of the hippocampus to be significantly engaged, relative to a control condition in which participants imagined isolated static objects⁴¹ (FIG. 2a). Specific increases in amHipp activity were found in another study in which subjects constructed and elaborated upon past events and imagined future events⁴² (FIG. 2b). When participants recalled episodic memories and imagined fictitious events set in the past or the future (based on recombined elements from episodic memories), amHipp was again the only part of the hippocampus to be significantly engaged during imagination⁴³ and was part of a larger region that was activated during both imagination and recall (FIG. 2c), whereas activation of the posterior hippocampus was found to occur specifically during vivid recall of real memories. Only amHipp was found

Figure 2 | Activation of the anterior medial hippocampus during fMRI. The images show the results of a selection of functional MRI (fMRI) studies in which the anterior medial hippocampus (amHipp; indicated by arrows) was engaged by imagination and recall (panels a–f) and visual perception (panels g–i) of scenes and events. Coloured regions are those in which there was an increased haemodynamic response during each task (in panel g, colours represent the percentage of subjects ($n = 34$) with activation, in the range of 50–80%). The tasks involved constructing static atemporal scenes⁴¹ (panel a), constructing and elaborating upon imagined events⁴² (panel b; white circle indicates the hippocampus), recalling past events and imagining events set in the past and future⁴³ (panel c), imagining specific rather than general future events⁴⁴ (panel d), autobiographical memory retrieval^{45,46} (panels e and f), viewing novel scenes relative to scrambled images⁶⁶ (panel g), viewing scenes in which an object had been moved relative to the background⁶⁷ (panel h; white circle indicates the hippocampus) or correct versus incorrect scene oddity judgements⁶⁹ (panel i). The overlap in activity between the perception and imagination of scenes is shown in panel j. Hippocampal activation for scene perception relative to object perception is shown in red, activity for imagining scenes versus imagining objects is shown in blue, and the overlap is shown in turquoise (also shown in sagittal and coronal slices)⁴⁷. Panel a is adapted from REF. 41, republished with permission of the Society for Neuroscience, from Using imagination to understand the neural basis of episodic memory, Hassabis, D., Kumaran, D. & Maguire, E. A., *27*, 2007; permission conveyed through Copyright Clearance Center, Inc. Panel b is adapted with permission from REF. 42, Elsevier. Panel c is adapted with permission from REF. 43, Elsevier. Panel d is adapted with permission from REF. 44, Wiley. Panel e is adapted with permission from REF. 45, Elsevier. Panel f is adapted from McCormick, C., St-Laurent, M., Ty, A., Valiante, T. A. & McAndrews, M. P., Functional and effective hippocampal–neocortical connectivity during construction and elaboration of autobiographical memory retrieval, *Cereb. Cortex*, (2015) **25** (5): 1297–1305, by permission of Oxford University Press. Panel g is adapted with permission from REF. 66, Wiley. Panel h is adapted from REF. 67, republished with permission of the Society for Neuroscience, from Double dissociation between hippocampal and parahippocampal responses to object-background context and scene novelty, Howard, L. R., Kumaran, D., Ólafsdóttir, H. F. & Spiers, H. J., **31**, 2011; permission conveyed through Copyright Clearance Center, Inc. Panel i is adapted from REF. 69, Lee, A. C. H., Brodersen, K. H. & Rudebeck, S. R. Disentangling spatial perception and spatial memory in the hippocampus: a univariate and multivariate pattern analysis fMRI study, *J. Cogn. Neurosci.* **25**, 534–546 (2013), reprinted by permission of MIT Press Journals, © 2013 Massachusetts Institute of Technology. Panel j is adapted from Zeidman, P., Mullally, S. & Maguire, E. A., Constructing, perceiving, and maintaining scenes: hippocampal activity and connectivity, *Cereb. Cortex*, (2015) **25** (10): 3836–3855, by permission of Oxford University Press.

to respond more strongly to imagining specific past or future events rather than general events (FIG. 2d), whereas the anterior lateral hippocampus distinguished past from future episodes⁴⁴. Autobiographical memory retrieval was also found to engage only amHipp⁴⁵ (FIG. 2e), although other subregions of the hippocampus were responsive to whether retrieval was cued using a direct association with the cue or a strategy of searching through memories. A subsequent study sought to distinguish the initial construction stage of autobiographical memory recall from elaboration⁴⁶, and within the hippocampus found solely amHipp engagement for construction (FIG. 2f). The posterior hippocampus was engaged during elaboration, which connectivity analyses showed was also linked to areas processing visual stimuli. These studies suggest that despite different research questions, tasks and some points of divergence — including the extent of differences between recalling the past and imagining the future⁵⁵ and the relationship between imagination, novelty and encoding (BOX 3) — one common feature across studies was the engagement of amHipp, in addition to regions of the wider core network^{42,53,54,56}.

The hippocampus may contribute to performance in these tasks by linking elements of scenes in a coherent spatial

representation, as suggested by studies in humans with bilateral hippocampal lesions. Self-reports from these patients demonstrate that they can fully comprehend the elements that should appear in an imagined scene but cannot arrange them into a spatially coherent representation^{39,40}. In one study, patients and control participants were asked to describe what they would see beyond the edges of a scene photograph⁴⁰. The patients described relevant objects that they would have expected to see, demonstrating preserved associational processing, but were specifically unable to describe how the extended scene would fit together and reported being unable to visualize it in their imagination. In another study³⁷, patients with bilateral hippocampal damage were tested on their ability to reflect on ‘what might have been’. The patients could deconstruct a given narrative and then add, recombine and re-order narrative elements into a counterfactual alternative reality. However, detailed questioning showed that they had specific impairment in the spatial coherence of the mental representations needed to perform some aspects of the task. Although these patients rarely, if ever, have lesions limited to the anterior hippocampus, these findings have been instrumental in demonstrating a spatial scene-related role for the human hippocampus.

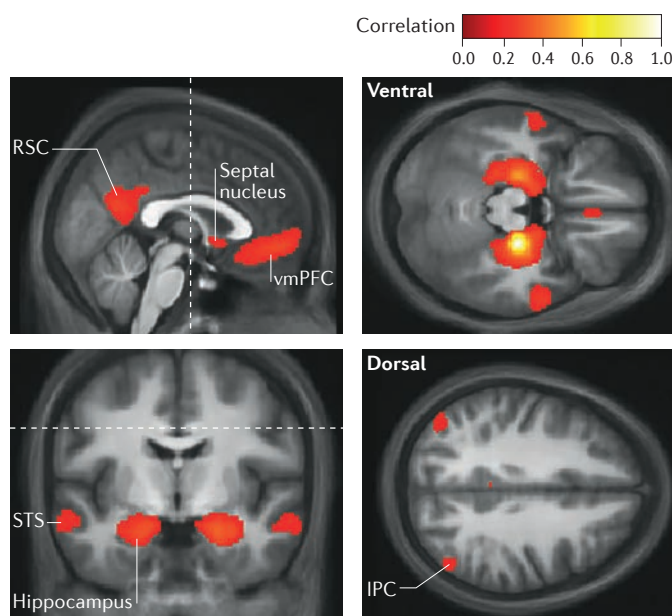
Visual perception and the posterior hippocampus. If the hippocampus is required for the internal representation of spatially coherent scenes or events, then it may also support perception by representing the environment currently being experienced. This contrasts with a long-standing theory of the hippocampus⁵⁸, which holds that the human medial temporal lobe (including the hippocampus) is involved only in memory and that perception involves a separate system. Over the past two decades, this proposed separation has been challenged by converging functional and anatomical results across species (for reviews, see REFS 11,59,60).

Investigations into hippocampal involvement in scene perception have focused on visual discrimination studies, in which subjects decide whether visually presented stimuli are identical or subtly different from each other or from a sample stimulus. Patients with bilateral hippocampal lesions cannot match morphed pictures of scenes to a sample but do not show this impairment when other stimuli are used, such as faces and objects⁶¹. Responding to criticism that this effect may be driven by learning over trials, a subsequent study⁶² used trial-unique stimuli in an odd-one-out task. The patients had difficulty in identifying non-matching scenes; however,

Box 2 | A core network for recall and imagination

A recent study⁴⁷ showed that recalling and imagining scenes activates the anterior medial hippocampus (amHipp) as part of a well-established ‘core network’ of brain regions⁵⁶. There are various suggestions as to what common function this network may serve^{56,104,105}. It is similar to a set of regions found to be most active during rest periods, termed the ‘default mode network’ (DMN)¹⁰⁶. The figure shows resting-state fMRI activity (based on 1,000 subjects at rest^{107,108}, accessed via the [Neurosynth](#) meta-analysis tool¹⁰⁹ — see Further information), illustrating **regions that had activity that correlated with that of the right amHipp**. The colour scale indicates the strength of the correlations (Pearson correlations (r)) between the blood oxygen level-dependent (BOLD) time series in each voxel and a seed voxel in the right amHipp (seed MNI coordinates 22, -20, -18; $r > 0.2$). This demonstrates the association between the DMN and amHipp. The DMN brain regions shown are the anterior superior temporal sulcus (STS), inferior parietal cortex (IPC), retrosplenial cortex (RSC), ventromedial prefrontal cortex (vmPFC) and the septal nuclei. In agreement with other authors¹¹⁰, we suggest that scene-related tasks such as recalling the past engage a similar set of brain regions as the DMN because they depend on common cognitive processes. When at rest, people often construct spatially coherent scenes, which may be generated in their imagination or recalled from their past. This gives rise to several testable predictions regarding the brain at rest. As patients with hippocampal lesions cannot imagine fictitious scenarios^{39,40}, their mind-wandering behaviour should be limited to events in the present. Moreover, these individuals should show changes within

the DMN compared with healthy control subjects. Indeed, changes in the DMN have been reported in amnesic patients with bilateral medial temporal lobe damage¹¹¹.



Box 3 | Other functions of the anterior hippocampus

Evidence points to the hippocampus being a site of integration between spatial and non-spatial information. There are several key themes in the literature implicating the anterior hippocampus.

Anxiety and stress. The anterior (ventral) hippocampus is associated with anxiety across species¹¹². Contextual fear conditioning, in which a spatial location is associated with an aversive stimulus, is associated with activity in the anterior hippocampus in humans^{113,114} and rodents (reviewed in REF. 115). The anterior dentate gyrus (DG) is the source of adult-born stem cells in the hippocampus¹¹⁶, and stress-related decreases in neurogenesis in primates are accompanied by increases in depressive symptoms¹¹⁷. However, neuroimaging studies in humans that have tested for changes in hippocampal volume associated with depression suggest that there are more often changes in the posterior than the anterior volume^{118,119}, potentially because neurogenesis effects are more difficult to measure in the anterior hippocampus¹¹⁹.

Novelty and encoding. The anterior hippocampus responds to novelty, particularly of spatial stimuli. For instance, there is a stronger response to novel scene stimuli than to those that are more familiar^{120,121}, and the anterior hippocampus also responds to novel spatial configurations⁶⁷. Moreover, it is engaged by associative novelty, in which novel stimuli are paired with familiar stimuli to form new associations or to violate expectations¹²². It has also been suggested that the anterior hippocampus is involved with encoding memories¹²³ and has been found to respond more strongly to imagined scenarios that are subsequently remembered than to those that are forgotten¹²⁴. However, successful encoding is not a prerequisite for anterior hippocampus engagement⁶⁹ or for its interaction with the core network¹²⁴ (BOX 2) in response to scene or event stimuli.

Decision making. Although beyond the scope of this article, the anterior hippocampus is associated with decision making and representation of value — functions that might relate to its anatomical connections with the prefrontal cortex. For instance, the anterior hippocampus and amygdala were found to represent value- and task-specific goals in spatial decision making^{125,126}.

Summary. Here, we build upon the proposal that the hippocampus constructs representations of scenes⁵². This will necessarily occur when a stimulus is novel or not recently recalled, and may integrate non-spatial elements, including emotional valence.

this impairment was only apparent when the scene pictures were taken from different viewpoints. By contrast, they were able to match pictures of faces regardless of the viewpoint. This is important because matching scenes from different viewpoints requires an internal global scene model, which we suggest is represented in the hippocampus. However, these results were not replicated in a separate group of subjects⁶³, and another study involving four patients found only two to have impaired perception of the topology of virtual reality scenes⁶⁴. Differences in the nature and extent of intra-hippocampal damage may help to explain these disparate functional outcomes⁶⁵ and emphasize the need to better understand intra-hippocampal anatomy and its mapping to function.

In healthy participants, the hippocampus consistently responds to visually presented scenes. Making an indoor versus outdoor decision about scene photographs was sufficient to engage much of the length of the hippocampus, with the most consistent result across subjects found to be in amHipp⁶⁶ (FIG. 2g). In another study, when the spatial configuration of items within visually presented scenes was altered, amHipp was activated⁶⁷ (FIG. 2h) together with a more anterior lateral region of the

hippocampus. This study did not identify posterior hippocampus activation. However, the posterior hippocampus was engaged during a scene discrimination task⁶⁸, and subregions of the hippocampus responded to viewing of scenes, regardless of whether they were subsequently recalled⁶⁹ (FIG. 2i), suggesting that the activation of the posterior hippocampus does not depend on memory encoding. To probe which aspects of scenes the hippocampus responds to, a task was developed^{70,71} in which scene discrimination based on global layout ('strength-based perception') was dissociated from discrimination based on local visual features ('state-based perception'). The posterior hippocampus was involved specifically with strength-based perception, reinforcing the notion that it represents the configuration of the scene as a whole. Beyond discrimination studies, a recent experiment had participants passively view scenes and single isolated objects as they underwent fMRI scanning⁴⁷. Activation of both amHipp and the posterior hippocampus was observed in response to perception of scenes, relative to perception of isolated objects. When the same participants constructed scenes in their imagination, there was significant engagement of amHipp without evidence for posterior hippocampus activity. Thus,

the posterior hippocampus appeared to be particularly responsive to visual scene perception rather than imagination, whereas amHipp was engaged by scenes regardless of whether they were generated internally or externally (FIG. 2j). This study also showed that amHipp was engaged by novel scenes, whereas the posterior hippocampus was engaged regardless of novelty, supporting the hypothesis that amHipp is involved with constructing an initial representation of the scene, whereas the posterior hippocampus has a more specific visuospatial role.

Also of relevance to scene perception is 'boundary extension' (BE)⁷², a cognitive phenomenon whereby people remember seeing more of a scene than was actually present in the original stimulus. This effect is attenuated in patients with hippocampal lesions⁴⁰ (see also REFS 65,73). Of note, during an fMRI study in which healthy participants viewed scenes and experienced BE in one-half of the trials, there was greater engagement of the posterior hippocampus during the viewing of scenes that induced BE⁷⁴. The BE effect was not linked with amHipp activity during neuroimaging, potentially because scene perception (which was present in all conditions) always engages amHipp, regardless of whether BE is experienced.

The evidence that the hippocampus is engaged during scene perception is challenged by studies of patients with hippocampal lesions who can lucidly produce narratives to accompany visually presented cartoon images or photographs^{40,75}. However, impairments become apparent when patients are asked to extend the scene beyond the edges of the picture into the imagination⁴⁰. This suggests that a hippocampus-based model of the scene, which is constructed during visual perception, facilitates prediction beyond the edges of the view as well as beyond the sensory domain into imagination and recall. We predict that asking patients with hippocampal lesions challenging questions about visually presented scenes that could only be answered by possessing a coherent internal scene model might reveal impairments that are not evident in more general narrative description tasks.

The tasks that we have discussed, which tap into apparently distinct cognitive functions, share a common requirement to form internal representations of spatially coherent scenes. This, we suggest, involves amHipp. The existence of amHipp as a distinct functional region was noted in a recent fMRI study⁴⁷ and lately by two studies that parcellated the hippocampus

based on a meta-analysis of fMRI data⁷⁶ and functional connectivity⁷⁷. The posterior hippocampus responds particularly strongly to visual scene perception, which may relate to its direct anatomical connections with the parahippocampal and retrosplenial cortices⁷⁸. How involvement of the posterior hippocampus with scene perception relates to its known role in navigation⁷⁹ is yet to be investigated. Interestingly, posterior hippocampal volume has been found to be reduced in blind people^{80,81}, with concomitant volume increases in the anterior hippocampus^{81,82} (although there are various possible explanations for this, such as differences in the navigation performance of blind people⁸²).

In suggesting functional differences between the anterior and posterior hippocampus, it is important to note that these functions are not completely segregated. For instance, although the posterior hippocampus responds more strongly to visual perception of scenes than imagination of scenes⁴⁷, there is evidence that it is engaged by imagination and recall^{48,49}. All of these functions involve extrinsic connections that link the hippocampus to parahippocampal and perirhinal cortices^{83,84}. There is also variability in the locus of hippocampal activation between studies, which may be explained by multiple factors, including the time that has lapsed since the stimuli to be recalled were first experienced^{48,50}, differences in task demands, differences in the definition of anterior versus posterior hippocampus and varying statistical thresholds. This variability, we suggest, makes the striking overlap in amHipp across studies all the more interesting.

From scenes to subfields

To investigate which specific structures underlie the activation patterns observed in amHipp in neuroimaging studies, an experiment was recently conducted³⁰ in which subjects constructed novel naturalistic scenes in their imagination and recalled scene photographs from a week earlier while undergoing high-resolution structural MRI and fMRI. The anterior presubiculum/parasubiculum (either or both) were activated by tasks specifically involving the construction and recall of scenes. There was also activation of the uncus when subjects recalled scenes first viewed a week earlier, and of the anterior subiculum when subjects constructed novel scenes. Effect sizes in the anterior lateral hippocampus and the posterior hippocampus were far smaller.

These results suggest that the engagement of amHipp in the studies using scene or event stimuli described above is likely to have been driven by activity in the presubiculum and parasubiculum, potentially in conjunction with the anterior subiculum and the uncus.

Anterior presubiculum and parasubiculum.

The presubiculum/parasubiculum were engaged by both scene construction and scene recall⁵⁰. These findings complement those of another recent fMRI study in humans, which identified the peak activity for perceiving novel scenes to be in the presubiculum⁸⁵. In rats, the presubiculum and parasubiculum contain grid cells and border cells²³, pointing to a spatial role for both regions. In monkeys, neurons in the presubiculum at the level of the uncus project to the medial EC¹⁸, which is commonly associated with spatial function and where grid cells were first discovered in rodents^{22,86}. On the basis of these findings, we hypothesize that the presubiculum/parasubiculum contribute to the spatial basis of scene representations in humans.

Uncus. As described above⁵⁰, the uncus is engaged when recalling scenes from a week before scanning. Although subfields within the uncus were not distinguished owing to the limited spatial resolution of MRI, one striking property of this region is its inter-hemispheric connectivity. In non-human primates, the uncus of hippocampus sends and receives commissural connections¹⁸, which complement the even stronger commissural connections arising from the presubiculum and terminating in the contralateral medial EC. Little is known about the precise differences in hippocampal function between hemispheres beyond suggestions of general verbal or visuospatial distinctions⁸⁷, and the homology of inter-hemispheric connections between humans and primates is uncertain²⁰. However, we speculate that recall of consolidated representations from memory may involve the integration of information from across regions located in both hemispheres and thus may be supported by connections that terminate in the uncus.

The uncus is also well placed to mediate communication between the prefrontal cortex (PFC) and the rest of the hippocampus. In non-human primates, subfield CA1' mainly projects directly to the PFC, particularly medial areas Brodmann area 25 (BA25)^{83,88} and BA14 (REF. 88), with fewer projections to the orbital PFC. There is an indirect pathway between CA1'

and the PFC via the amygdala: both the prosubiculum and CA1' project to the basal nucleus⁸⁹, which in turn projects widely through the medial PFC (BA24, BA25 and BA32), lateral PFC (BA12 and BA45) and orbital PFC (BA7a, BA13b and BA14)⁹⁰. Functional neuroimaging studies in humans have also found that the PFC, particularly the ventromedial PFC, is co-activated with the anterior hippocampus (BOX 2). Of particular relevance are studies that implicate the ventromedial PFC in memory consolidation^{48,91,92}. Thus, the uncus and ventromedial PFC may be jointly involved in retrieving the elements of memories that have been consolidated, to be reconstructed as spatially coherent scenes by amHipp.

Anterior subiculum. The subiculum is the main output structure of the hippocampus (although there are outgoing connections from various other parts of the hippocampus⁹³). This region includes border cells²⁶, pointing to a role in modelling the environment. The anterior subiculum is engaged when subjects imagine novel scenes⁵⁰. In human fMRI, the subiculum and prosubiculum are not generally distinguishable but differ in their connectivity. The subiculum projects to the mammillary bodies and retrosplenial cortex¹², two regions that are closely involved with the representation of head direction. The prosubiculum, however, has reciprocal connections with targets including the ventromedial PFC¹².

Methodological issues. The anterior hippocampus is particularly challenging to study using fMRI. A consensus has not yet been reached on the definition of the subfields at the resolution attainable with MRI, although work is underway⁶. Weak contrast-to-noise ratio is a well-known problem in the anterior temporal lobes and may cause false negative results. Furthermore, the uncus is flanked by significant vasculature⁹⁴. The influence of vasculature on fMRI interpretation has been questioned⁹⁵, but this issue is not specific to the hippocampus. These concerns emphasize the importance of having well-matched control conditions, the need for precise anatomical detail as well as the necessity of further research into neurovascular coupling.

A model and future directions

On the basis of the available anatomical and functional data, we propose that the hippocampus (specifically amHipp) supports modelling of scenes. It can be driven 'offline'

during imagination and recall in order to construct a spatially coherent scene representation. In addition, it continually constructs and refines a representation of the scene being experienced 'online', extending into the perceptual domain the notion of scene construction^{51,52}. The presubiculum and parasubiculum provide a spatial basis for the elements of the scene, complemented by the uncus and anterior subiculum, which may mediate communication with other regions that represent the elements of the scene and generate vivid imagery. When visual stimulation is used to update one's internal model, or when visual representations are vividly reinstated during recall, the posterior hippocampus is additionally engaged to process the visuospatial properties of the scene.

This model makes several predictions. First, there should be a greater response to novel than familiar scenes in the anterior hippocampus, reflecting the construction of the novel representation. This is supported by many findings² (BOX 3) and helps to explain why scene novelty particularly engages amHipp^{47,67}. Second, amHipp should be engaged when a spatially coherent representation of a scene needs to be constructed or used for simulating events. This is borne out by recent findings, including those of studies using simple visual scene perception tasks^{47,66} as well as scene discrimination tasks, in which patients with hippocampal lesions could distinguish scenes from the same angle but not different angles⁶². Third, amHipp will be placed under greater demand for recalling consolidated memories than very recent memories, because in the former case the scene must be constructed from a distributed representation across the cortex. A recent study found a greater amHipp response to recall of scenes encoded a week before scanning than to scenes encoded 30 minutes before scanning⁵⁰. Consolidation findings do, however, differ across studies, which have used varying stimulus content, analysis techniques and durations of consolidation^{48,50,92,96–98}. We argue that exploring the role of the uncus in recall will be key to understanding these differences. Last, the model predicts that patients with bilateral hippocampal lesions will have visual perceptual deficits, but only when probed in such a way as to demand a coherent internal model of their surroundings. More detailed neuropsychological studies should be able to evaluate the limits of visual scene perception in the presence of dysfunctional hippocampi.

By reformulating the current 'perception versus memory' debate with reference to the detailed anatomy of the anterior hippocampus, we believe that increased explanatory power and more fruitful lines of inquiry can be forthcoming. Moreover, this proposal may help to clarify the discussion about functional differences along the long axis of the hippocampus, as well as provide the anatomical detail needed to refine computational models of hippocampal function. For instance, one computational model of spatial memory and imagery⁹⁹ proposed that CA3 combines spatial information from boundary vector cells with object identity information in the perirhinal cortex to facilitate pattern completion. The findings summarized here suggest that this point of integration between spatial and non-spatial information may be the presubiculum and/or parasubiculum in humans.

In our opinion, visual perception, imagination and episodic recall depend on a common process: the creation of models of the world and the use of those models to plan scenarios and replay memories. This hypothesis, we suggest, offers a better way to understand the function of the hippocampus and to reconcile apparently disparate findings in the literature. Nevertheless, there are numerous unanswered questions. What form does the spatial representation in the presubiculum and parasubiculum take? What visually driven operations are performed by the posterior hippocampus and how do these relate to navigation? Most of all, we call for further studies capitalizing on advances in high-resolution fMRI in humans to understand the specific functional anatomy of the anterior hippocampus as well as its functional connectivity with neighbouring structures. The uncus is particularly poorly understood, but the results reviewed here suggest that it may have an important role in scene recall. High-resolution neuroimaging experiments and analysis of gene expression¹⁰⁰ in humans could complement neuropsychological studies of patients and *in vivo* animal models to improve our knowledge of this critical brain region.

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Competing interests statement

The authors declare no competing interests.

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