

Parahippocampal and retrosplenial contributions to human spatial navigation

Russell A. Epstein

Department of Psychology and Center for Cognitive Neuroscience, University of Pennsylvania, 3720 Walnut Street, Philadelphia, PA 19104-6241, USA

Spatial navigation is a core cognitive ability in humans and animals. Neuroimaging studies have identified two functionally defined brain regions that activate during navigational tasks and also during passive viewing of navigationally relevant stimuli such as environmental scenes: the parahippocampal place area (PPA) and the retrosplenial complex (RSC). Recent findings indicate that the PPA and RSC have distinct and complementary roles in spatial navigation, with the PPA more concerned with representation of the local visual scene and RSC more concerned with situating the scene within the broader spatial environment. These findings are a first step towards understanding the separate components of the cortical network that mediates spatial navigation in humans.

Introduction

The ability to find one's way through a large-scale space such as an airport, college campus or city neighborhood is essential for successful functioning in the modern world. Wayfinding was probably even more important to our phylogenetic ancestors, who could not have survived without the ability to navigate between locations that provided food, shelter and water. Neurophysiological studies in animals have greatly advanced our understanding of how this core cognitive function is implemented at the neuronal level by identifying several classes of cells that encode spatial quantities useful for navigation, including place cells in the hippocampus [1], head direction cells in Papez circuit structures [2] and grid cells in entorhinal cortex [3]. By contrast, the neural systems supporting spatial navigation in humans are less well understood.

Neuroimaging studies of human navigation most commonly activate the posterior parahippocampal and retrosplenial cortices [4–10], regions that also respond strongly during passive viewing of navigationally relevant visual stimuli such as scenes and buildings [11–14]. Consistent with these findings, damage to these areas often leads to wayfinding deficits [15]. These results indicate that parahippocampal and retrosplenial cortices are key nodes of the neuronal network that support spatial navigation in humans. But what are the specific functions of each of these nodes? In particular, what kind of navigationally relevant information processing does each region support?

Answering these questions is crucial if we are to understand how spatial navigation is mediated by the human brain. Previous reviews of spatial navigation have either focused on other brain regions [16–18] or have restricted themselves to the neuropsychological data [15]. Here, I focus specifically on the parahippocampal and retrosplenial cortices, reviewing recent results from neuroimaging, neuropsychology, neuroanatomy and neurophysiology that illuminate the crucial contributions these regions make to human spatial navigation.

The Parahippocampal place area

Basic properties

In 1998, Kanwisher and I [11] reported that a region at the boundary between posterior parahippocampal cortex and the anterior lingual gyrus that we labeled the 'parahippocampal place area' (PPA) responds preferentially to pictures of places. In particular, the PPA responds strongly to complex visual scenes such as landscapes or cityscapes, weakly to nonscene objects (e.g. appliances, animals and vehicles) and to scrambled images and not at all to faces [19] (Figure 1). The scene-preferential response in the PPA extends to a wide variety of scenes, including landscapes, cityscapes, rooms, tabletop scenes [20] and even 'scenes' made out of Lego blocks [21]. Although the PPA is sometimes referred to as a 'building' or 'house' area [13,14,22], its response to buildings is smaller than the response to scenes [11] and this response is further reduced when subjects are induced to treat a building as a discrete object rather than as a partial scene [21], indicating that scenes rather than buildings are the optimal stimulus.

PPA response to real-world scenes is only weakly affected by familiarity with the locations depicted in the scenes [21,23]. This indicates that the PPA is primarily involved in perception or encoding of the local scene, rather than higher-level mnemonic or navigational tasks [24]. However, it is important to note that a scene does not have to be visible for the PPA to respond. Like many high-level visual areas, the PPA activates during mental imagery, specifically imagery of places [25], which might account for PPA activity during mental navigation tasks [5–7]. Furthermore, PPA response to nonscene objects can be modulated by the navigational or contextual significance of the stimulus [26,27]. Thus, the PPA seems to respond not just when scenes are visible, but also when scenes are cued or brought to mind.

Corresponding author: Epstein, R.A. (epstein@psych.upenn.edu).

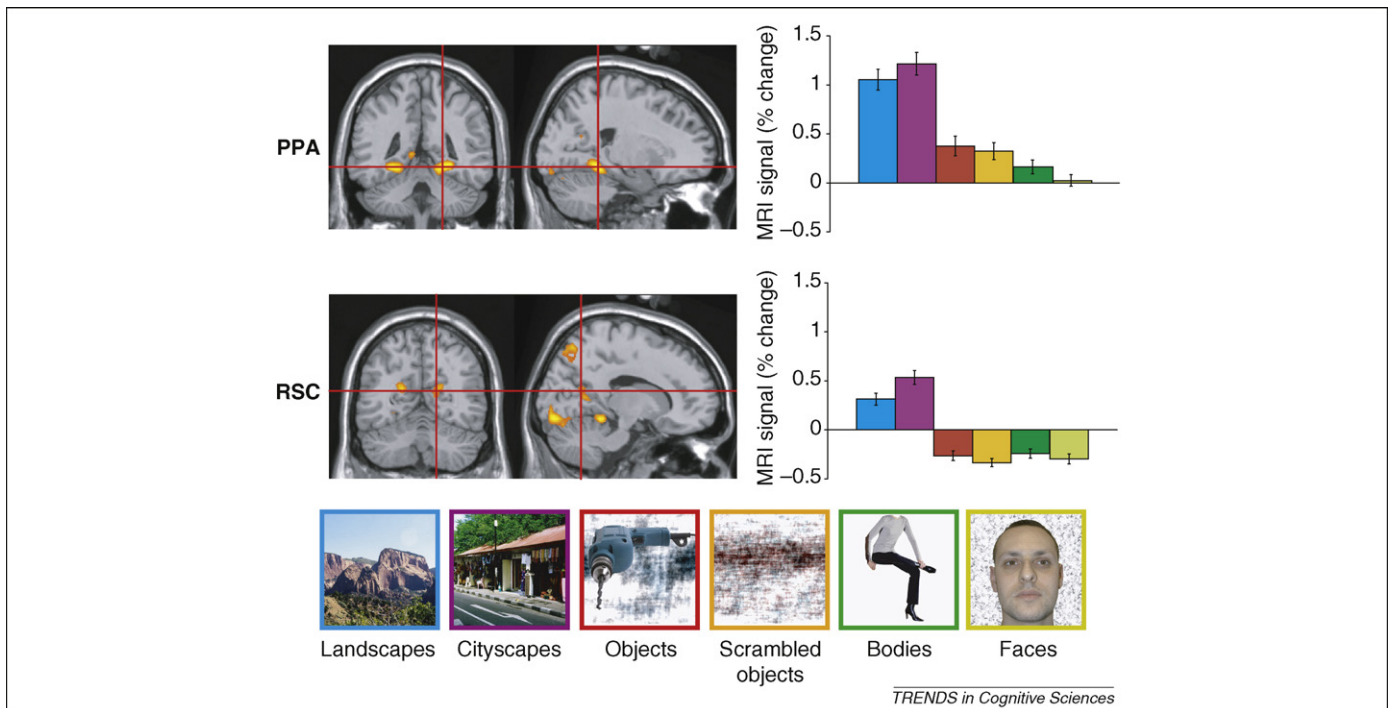


Figure 1. Location and basic response properties of the PPA and RSC. Brain maps showing the PPA and RSC are plotted on a reference anatomical brain in standard space. Orange voxels responded more strongly ($p < 0.05$, corrected for multiple comparisons) to scenes than to nonscene objects in a random effects group analysis ($n = 38$; previously unpublished). Crossbars indicate the location of the PPA and RSC. Bar charts show the response in the PPA and RSC to six stimulus categories, plotted as percent signal change relative to a fixation (no-stimulation) baseline. For this analysis, the PPA and RSC were functionally defined on each subject as described previously (e.g. Ref. [102]). PPA clearly responds most strongly to scenes, although it is not completely unresponsive to other stimuli. RSC response is significantly above baseline for scenes, but significantly below baseline for other stimuli.

The monkey homolog of the PPA is unclear. Although we have previously speculated that PPA is equivalent to the two cytoarchitecturally defined regions (TF and TH) that comprise macaque parahippocampal cortex [28], a recent report by Saleem and colleagues [29] indicates that it might make up only a subset of this larger parahippocampal region. These authors identified a subregion of posterior TF, which they label TFO, which contains a prominent layer IV, making it more functionally similar to adjoining visually responsive regions such as V4 and TEO than to the more anterior parts of parahippocampal cortex. The remainder of TF and TH might have a more general role in spatial memory (Box 1).

Neuropsychological studies

The parahippocampal and lingual territory encompassing the PPA is often damaged in posterior cerebral artery strokes, leading to problems with wayfinding [30], particularly when the damage is in the right hemisphere. Typically, these patients report that they cannot identify large topographical entities such as streets, buildings or intersections, although they can determine the general semantic class to which these entities belong [31]. Sometimes they will compensate for this impairment by focusing on small details (e.g. a mailbox or a street sign) [32]. Their understanding of the spatial relationships between different locations is often preserved; thus, they can draw maps of the route they would take between different locations even though their recognition deficits prevent them from implementing these routes in the real world [33,34]. Although at first glance their visual perception is unimpaired (with the common exception of a visual field cut),

these patients often complain that some global organizing aspect of the scene is missing [35–37].

Mendez and Cherrier [33] examined a typical patient (GN), whose wayfinding was impaired in both familiar and unfamiliar environments. GN had particular difficulties in nondescript environments such as corridors, public bathrooms and theaters, reporting, for example, that ‘things look so similar in bathrooms; they all look all white’. When asked to identify prominent landmarks (e.g. buildings) and scenes (e.g. intersections) along a route, landmark recognition was normal but his ability to identify scenes that did not contain a single prominent object-like landmark was severely impaired (Figure 2a). Interestingly, if he was able to recognize a landmark or scene, he knew which direction to go from the landmark; indeed, he reported that he retained the equivalent of a ‘street guide’ of his hometown in his head. In sum, he was unable to recognize scenes as a whole, but was able to use his apparently undamaged object-recognition system to identify landmarks. The fact that his scene analysis problem was exacerbated in relatively featureless environments such as bathrooms might indicate that he has particular difficulties when scenes must be parsed solely on the basis of spatial geometry.

My colleagues and I observed similar deficits in two patients with parahippocampal damage, one of whom we were able to verify had no functioning PPA [36]. Notably, our patients found it exceedingly difficult to learn the topographical structure of new environments, presumably because of their inability to encode the local scene. By contrast, anecdotal evidence indicated that their spatial knowledge of pre-morbidly learned environments was more or less intact.

Box 1. Anterior parahippocampal cortex

Should the PPA be considered a single unit? There is some tantalizing, yet inconclusive, evidence for a functional division of labor between anterior parahippocampal cortex (PHC) and the posterior portion of the PPA (which extends into the lingual gyrus). In particular, anterior PHC might do more than just scene recognition; it might also have a more general role in spatial memory encoding [94]. This hypothesis rests on three lines of evidence. (Note that anterior PHC should not be confused with the anterior portion of the parahippocampal gyrus, which includes perirhinal cortex.)

- (i) Anatomical and connectivity data indicate that macaque region TFO can be distinguished from more anterior regions TF and TH. Although TFO seems to be a visually responsive region with a prominent layer IV, TF and TH might be more involved in spatial memory, combining inputs from both the ventral stream (V4, TE and TEO) and dorsal stream (retrosplenial, posterior parietal) before sending outputs to entorhinal cortex and the hippocampus [63,95]. The connectivity between parietal cortex and anterior parahippocampal regions is strong enough that damage to the latter can lead to visuospatial neglect [96].
- (ii) The neuropsychological literature points to a distinction between patients who have difficulties primarily in new environments [34–36] and others who have difficulties in both new and familiar environments [32–35,37]. Aguirre and D'Esposito [15] label the former syndrome 'anterograde disorientation' and the latter 'landmark agnosia', although they note that it is unclear whether these syndromes are entirely distinct. Anterograde disorientation might be caused by damage to a topographical learning mechanism in the anterior PHC, whereas landmark agnosia might occur when more posterior scene recognition mechanisms are damaged [34].
- (iii) Parahippocampal cortex is sometimes excised to treat intractable epilepsy. These patients typically have damage restricted to the anterior portions of the medial temporal lobe including anterior PHC, leaving undamaged the more posterior regions that are typically impacted in stroke patients. These epilepsy patients can exhibit problems on spatial memory tasks even when these tasks do not involve scene perception in any obvious way [97–99]. For example, Ploner and colleagues [100] found that patients with right parahippocampal lesions were impaired in their ability to remember locations in the left visual hemifield and to make saccades to those locations after delays of 30s.

An interesting contrast to GN is provided by DF, a patient whose PPA is preserved but whose object form processing pathway is almost completely obliterated [38]. Despite her inability to recognize objects, DF was able to classify scenes in terms of general categories such as city, beach or forest; furthermore, her PPA was activated when she performed these tasks. Taken together, GN and DF demonstrate a double dissociation between scene and object processing: the PPA seems to be part of a distinct processing stream for scenes that bypasses the more commonly studied object-processing pathway [39].

Information processing in the PPA

The data presented thus far indicate that the PPA is crucial for identification of visual scenes but do not indicate the specific representations used to mediate this function. For any visual recognition mechanism, we can ask two fundamental information-processing questions. First, what is the spatial reference frame that the mechanism uses to represent the recognized entity? Here, the answer seems to be that the PPA encodes scenes in an observer-centered (viewpoint-specific) rather than a world-centered (viewpoint-invariant) reference frame

Box 2. Viewpoint- and position-specificity of scene processing in the PPA

There are at least two coordinate frames that the PPA could potentially use for scene encoding: viewer-centered or scene-centered. In the former case, the PPA would separately encode different views of a given scene, whereas in the latter case a single representation would be encoded that could be accessed from different vantage points. My colleagues and I addressed this issue in a series of experiments by exploiting a phenomenon known as fMRI repetition suppression (fMRI-RS), which is the reduction of fMRI response obtained when stimuli are presented more than once. The key question was whether repeating a scene from a different viewpoint leads to a reduced response; if so, the two views of the scene must be (to some extent) representationally equivalent. We consistently observed fMRI-RS for same-viewpoint repetitions but not for different-viewpoint repetitions, arguing for viewpoint-specific processing [20,23,101,102]. Interestingly, some cross-viewpoint adaptation was observed when stimuli were repeated over longer time intervals [23,101,102] or when the viewpoint changes were part of an ordered sequence reflecting coherent motion around the scene [21,103]. However, even in these cases, complete viewpoint-invariance was never achieved.

A second basic question about any visual representation is the degree to which it is sensitive to the position of the stimulus on the retina. MacEvoy and I [104] found that RS effects in the PPA were insensitive to cross-midline changes in retinal position of up to 12 degrees, an amount of visual change to which object-selective regions such as the lateral occipital complex (LOC) were highly sensitive. These results indicate receptive fields in the PPA are larger than those in object-processing regions, which might reflect PPA involvement in the encoding of large, extended scene features such as walls or hillsides.

Taken together, the results of the viewpoint-invariance and position-invariance studies indicate that the PPA is sensitive to visual changes induced by movement of the observer around the scene (i.e. viewpoint changes), but insensitive to visual changes induced by eye movements (i.e. retinal position changes), which are less navigationally relevant. Similar results have been observed in RSC. However, this region seems to be somewhat less sensitive to specific perceptual details such as viewpoint [23] or scene framing [105]. Interestingly, despite neurophysiological and neuropsychological evidence for viewpoint-invariant place representations in the hippocampus [41,106], my colleagues and I have not observed consistent evidence for viewpoint-invariant fMRI adaptation in this region. This might simply reflect the fact that fMRI-RS effects in the hippocampus are somewhat recalcitrant (e.g. Refs [107,108], but see Ref. [109]) perhaps because neurons in this region have different inherent properties than those in neocortex. Alternatively, fMRI-RS in the hippocampus might depend more on explicit memory judgments that are shaped by task requirements than on stimulus repetition *per se* [110]. In particular, the extent to which the hippocampus considers two views of the same scene to be 'the same' or 'different' might depend on whether the task is to judge place repetitions or view repetitions (c.f. Ref. [111]), in contrast to the PPA in which fMRI-RS is driven by view repetition irrespective of task [112].

(Box 2). Second, what are the basic elements that the system uses to represent the entity? Here, the evidence indicates that the PPA does not encode every aspect of the scene; rather, it primarily encodes the spatial layout of the scene as defined by large fixed surfaces (Figure 2b). In other words, the PPA treats the entire scene as a unified object, distinct from its component elements, which can be encoded and recognized in its own right. This contrasts with the hippocampus, which seems to encode a qualitatively different representation of the scene, including information about specific objects and where they are located in space [40–44].

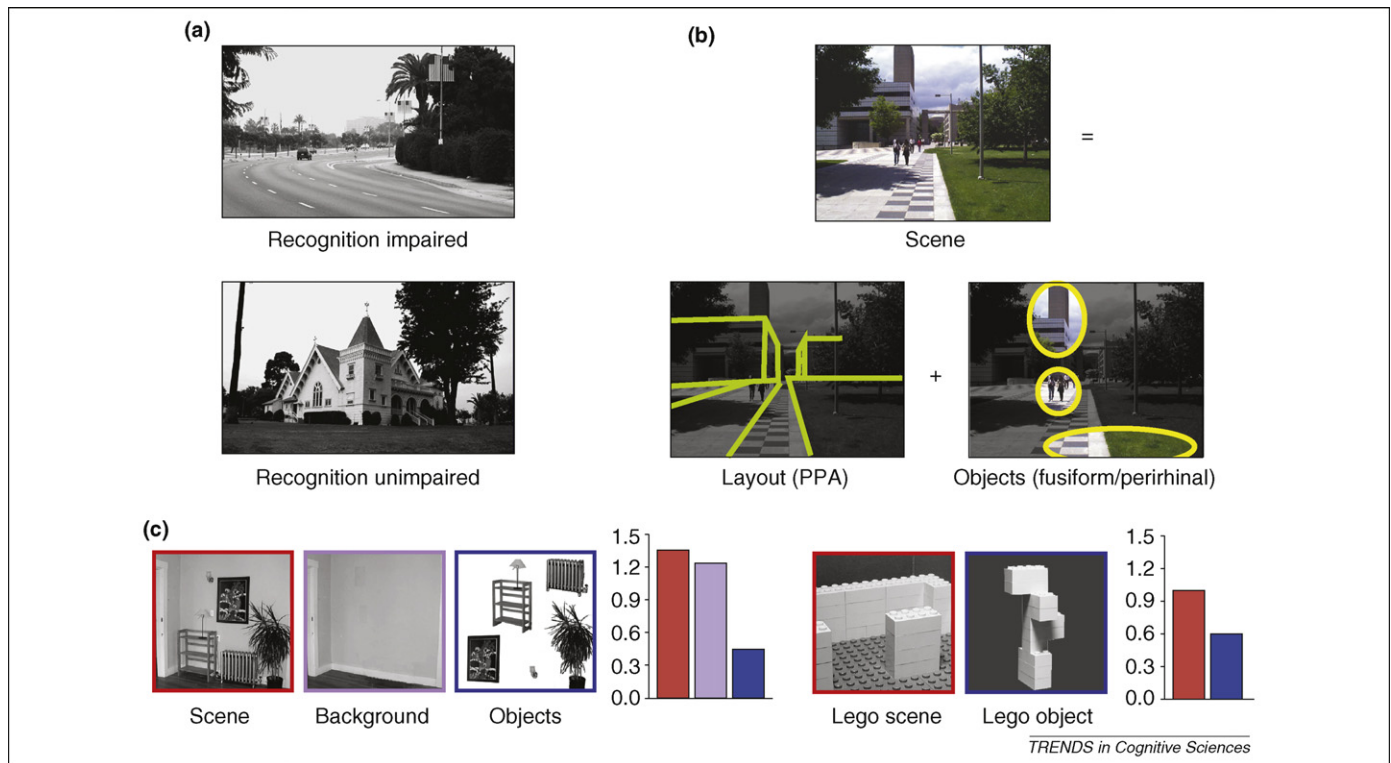


Figure 2. The PPA and scene encoding. (a) Neuropsychological evidence for PPA involvement in scene recognition. A patient with right hemisphere parahippocampal damage was unable to recognize scenes unless they contained a single prominent object-like landmark, indicating that patients with PPA damage can recognize large objects but not scenes *per se* [33]. (b) Under the spatial layout hypothesis, the PPA encodes the overall spatial layout of the scene as defined by fixed topological features, whereas information about the individual objects in the scene is encoded in the lateral occipital complex, fusiform gyrus and perirhinal cortex. When the PPA is damaged, patients report that they can see the objects in the scene but the overall organization of the scene is lost, indicating that normal scene perception involves the integration of object and layout information. (c) The PPA responds strongly to layout-defining scene features such as walls and ground planes. In particular, the PPA response to indoor scenes is not significantly changed by removing the objects, but is significantly reduced by removing the background [11]. Furthermore, PPA response to the Lego ‘scenes’ is significantly greater than response to Lego ‘objects’ [21]. Figure adapted, with permission, from Refs [11,21,33].

Supporting the spatial layout hypothesis is the fact that the PPA response to indoor scenes does not depend on the presence of discrete objects within the scene. The PPA responds equally strongly to empty rooms and rooms filled with furniture and objects, whereas its response to arrays of objects drawn from the rooms but displayed on a blank background is quite weak [11] (Figure 2c). Thus, the PPA seems to be driven primarily by fixed background elements such as walls, which define the geometry of local space, rather than by smaller objects within that space. (However, see Ref. [26] for an alternative view.) Subsequent studies have reported that the PPA responds more strongly to ‘scenes’ made out of Lego blocks than to ‘objects’ made out of the same materials [21,36] (Figure 2c). It also responds more strongly to full scenes (e.g. a kitchen) than close-up scenes (e.g. a close-up of the stove) or to scene-diagnostic objects (e.g. the stove with all background information removed) [45], and more strongly to scenes that retain their spatial organization than to scenes whose surfaces have been rearranged so that they no longer define a coherent 3D space [11]. These results indicate that PPA response is strongest to stimuli that provide the most information about the geometric structure of local space, even when other aspects of the stimuli are tightly controlled.

Although these results are consistent with the idea that the PPA encodes ‘spatial layout’, there are many different varieties of spatial layout that might be encoded. One

possibility is that the PPA encodes the geometry of the fixed elements of scene as ascertained from a particular point of view. For example, the PPA might encode a kind of ‘shrink-wrapped’ geometry of the scene akin to its surface shape, or a rough-and-ready representation of the major barriers and affordances within the scene. Alternatively, the PPA might be less concerned with encoding the scene itself than with processing the observer’s location and orientation relative to it [20], perhaps by first extracting information about the principal axes of the observed space. Some evidence for this last idea comes from a recent study that found that PPA activity during a learning episode did not depend strongly on the stimulus materials (ground-level versus aerial views of a scene) but did depend strongly on whether or not the observer had to keep track of a changing orientation relative to the scene [46].

Finally, an important unresolved issue is whether the PPA solely encodes geometric information, or whether it also encodes information about the distribution of visual features such as colors or textures within a scene [47]. The idea that the PPA encodes only geometry fits nicely with behavior studies indicating that animals and humans preferentially use the shape of local space to re-orientate when lost [48]. Indeed, ecological arguments indicate that fixed topographical elements such as walls, hillsides or pathways should be particularly important for place recognition because these are the aspects of a place that tend to be unchanging over time [49]. However, some recent evi-

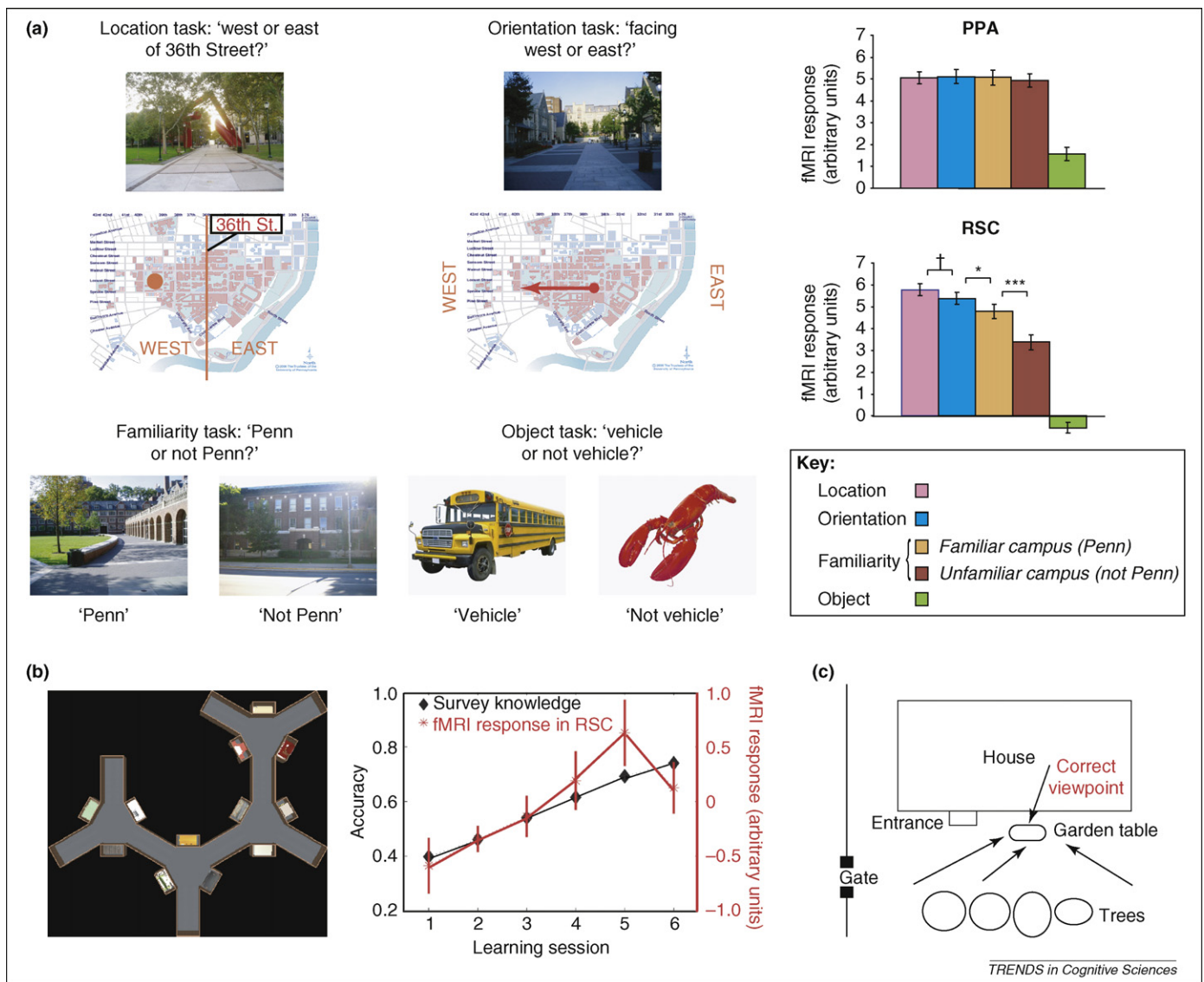


Figure 3. RSC supports retrieval of long-term spatial knowledge. **(a)** RSC activity corresponds to retrieval of long-term spatial knowledge. University of Pennsylvania students were scanned with functional magnetic resonance imaging (fMRI) while viewing photographs of their home campus (Penn), an unfamiliar campus or nonscene objects [24]. For the home campus photographs, they either retrieved spatial information (location or orientation) about each scene or made a simple familiarity judgment. RSC response was stronger during location or orientation judgments than during familiarity judgments. Furthermore, RSC response was higher when viewing images of the familiar campus than when viewing images of the unfamiliar campus, even when task was controlled. These results demonstrate that RSC response is stronger when viewing scenes whose spatial surroundings are known (Penn Images) than when viewing scenes whose spatial surroundings are unknown (Not Penn Images) and is even further enhanced when subjects explicitly retrieve long-term spatial knowledge (e.g. location, orientation). Note that PPA response was unaffected by task or familiarity, consistent with its proposed role in local scene perception. Abbreviations: †, $p < 0.06$; *, $p < 0.05$; ***, $p < 0.001$. **(b)** RSC activity during learning of a virtual-reality town increases in tandem with subjects' increasing survey knowledge about the town [58]. **(c)** RSC damage leads to an inability to understand the relationship between egocentric and allocentric representations. Here, one such patient was shown a photograph of the garden of her house, and was asked to determine the viewpoint from which the photograph was taken [74]. Her responses are indicated by arrows; the correct response is also noted. She was unable to perform this task accurately. Figure adapted, with permission, from Refs [24,58,74].

dence indicates that lingual and fusiform regions abutting the PPA are sensitive to material properties of objects such as color or texture [50], a finding that argues against purely geometric encoding in the PPA. One possibility is that different subregions within the PPA encode the geometric and nongeometric properties of the scene; however, at this point this idea is purely speculative.

The Retrosplenial complex

Basic properties

A second focus of cortical activity during navigation tasks is found in the retrosplenial cortex-posterior cingulate-medial parietal region, near to the point where the calcar-

ine sulcus joins the parietal-occipital sulcus. Retrosplenial cortex (BA 29 and 30) adjoins and is partially encircled by the posterior cingulate (BA 23 and 31) [51–56]; consequently, these labels are often used somewhat interchangeably when describing the locations of functional activations. Because of these ambiguities, I use the term retrosplenial complex (RSC) to refer to this functional-defined scene-responsive region, which is not necessarily identical to the anatomically defined retrosplenial cortex [26].

RSC is strongly active during scene viewing, scene imagery [25] and mental imagination of navigation through familiar environments [8]. In contrast to the

PPA, in which place familiarity effects are usually quite small, RSC responds 50% more strongly to familiar than to unfamiliar places [23,57], indicating that RSC is involved in recovery of long-term spatial knowledge about familiar environments. Further evidence for this idea comes from recent studies reporting that RSC activity was significantly greater when subjects reported the location of a campus scene than when they simply reported whether it was familiar or not [24] (Figure 3a) and that RSC activity during learning of a virtual-reality town corresponded to the total amount of survey knowledge acquired [58] (Figure 3b; see also Ref. [59] for similar results in mice). Although RSC has often been described as being part of a 'default network' because it tends to deactivate during a variety of cognitive tasks [60], its response to scenes is significantly above baseline, reflecting true involvement in scene processing rather than simply an absence of disengagement for these stimuli (Figure 1).

Anatomical connectivity data are also consistent with the idea that RSC supports spatial memory. In the monkey, the retrosplenial cortex and posterior cingulate are strongly interconnected with parietal region 7a and the lateral intraparietal (LIP) area, in addition to medial temporal regions such as entorhinal cortex, pre-subiculum, post-subiculum and parahippocampal regions TF and TH [52,61–63]. Thus, RSC is well-positioned to translate between egocentric spatial codes in the parietal lobe and allocentric spatial codes in the medial temporal lobes [64,65]. Projections from the anterior thalamus [55,66] and dorsolateral prefrontal cortex [52,55] might provide crucial head direction and working memory inputs that help mediate this translation [67]. Similar anatomical connectivities are found in rats [68,69].

Neuropsychological data

Navigational difficulties are frequently reported when the retrosplenial region is damaged by stroke in humans [70–77] or lesioned in rats [78]. Often, the onset of the impairment is quite dramatic. For example, one patient suddenly became lost while returning home from work: 'he could recognize buildings and the landscape and therefore understand where he was, but the landmarks that he recognized did not provoke directional information about any other places with respect to those landmarks. Consequently, he could not determine which direction to proceed' [71]. Such navigational difficulties have been reported after lesions affecting the right hemisphere [70,72,74,75], left hemisphere [71,75,77], both hemispheres [76] and retrosplenial white matter [73]. Interestingly, these problems often clear up after a few months with unilateral damage [70,75], but not bilateral damage [76], possibly because the undamaged hemisphere begins to compensate in the unilateral case [71].

In contrast to parahippocampally damaged patients, retrosplenially damaged patients report that they can identify scenes, but they cannot use them for purposes of orientation. Because of this deficit, these patients are unable to find their way, even in quite familiar environments. When asked to draw or label maps of their neighborhood or floor plans of their house, most are unable to do so [70,71,73,76,77] (but see Ref. [74]). A few can verbally

recount the routes that they cannot successfully implement [74,75], but most cannot [70,71,73,76,77]. Although they can sometimes describe what one would expect to see from a particular vantage point [72,74] they cannot determine the spatial relationship between two locations if one cannot be seen from the other [70].

As might be expected given the anatomical connectivities of the region, a key element of the retrosplenial syndrome seems to be an inability to translate between egocentric (viewpoint-dependent) and allocentric (survey-level) representations. For example, one patient was completely unable to use a map to indicate her viewpoint relative to her house [74] (Figure 3c), and another could not identify her current position within a room by pointing to a floor plan or a miniature model of the room [72]. Others could not follow a route within a room if this required them to make changes in orientation [71,73]. This inability to convert back and forth between egocentric and allocentric representations might severely impact navigation by making it impossible to relate the local scene to an allocentric spatial representation such as a cognitive map.

Information processing in RSC

Although the results described indicate that RSC supports mechanisms that enable us to situate ourselves in global space, little is known about the specific representations that the RSC uses to mediate these mechanisms. Rodent neurophysiological studies indicate that RSC neurons can encode a variety of spatial quantities such as head direction (HD cells) [79] and head direction while in a particular location (direction-dependent place cells) [80]. However, it is currently unclear whether these different varieties of cells are found within the same region or distinct retrosplenial subregions. Neither is it clear whether these cell types are found in human RSC as defined by functional imaging studies.

Keeping these caveats in mind, I can offer some speculations about information processing in RSC during navigation. In a recent neurophysiological study, Sato and colleagues [81] recorded from medial parietal neurons (i.e. possibly RSC) while monkeys followed well-learned paths through a multi-room virtual-reality environment. Of the many neurons that responded strongly during this task, 77% responded specifically when the animal made a particular action (turn left, right or move forward) at a particular location. One possible interpretation of these results is that the neurons encoded the bearings from each location to the next point in the path. Sato and colleagues [81] did not attempt to distinguish between egocentric and allocentric bearings ('turn to the left' versus 'turn to the east'); however, results from delayed-saccade experiments indicate that neurons in this region encode target locations in both coordinate frames [82]. Interestingly, many of the neurons in Sato and colleagues' [81] study responded in a path-selective manner, indicating that, at least during the initial stages of learning an environment, RSC distinguishes between paths even when they pass through the same location.

These results are consistent with the idea that RSC supports representations that enable 'you are here' infor-

mation to be translated into ‘your goal is to the left’ (in addition to the opposite, egocentric-to-allothetic translation), an idea that draws additional support from the neuropsychological data indicating that RSC patients cannot determine the direction to unseen goals. In a recent report, Byrne *et al.* [67] propose a computational model of how this transformation might be performed, in which RSC uses heading direction inputs from the thalamus to compensate for the rotational offset between the egocentric and allocentric coordinate frames [67]. In addition, it could be hypothesized that RSC is more than just a device for translating between hippocampal and parietal spatial codes. It might also encode its own representation of the spatial structure of the world which might be sufficient to support some kinds of navigation when the hippocampus is damaged [83,84] or in simple and/or very familiar environments [85]. Specifically, by encoding routes or bearings between prominent locations, RSC might support a topological graph [86,87] that supplements the more metrical and detailed cognitive map supported by the hippocampus and entorhinal cortex [17,88].

Conclusion: two processing streams for visually guided navigation?

The PPA and RSC seem to have distinct but complementary roles during spatial navigation. The PPA encodes a representation of the local scene that enables it to be remembered and subsequently recognized, whereas RSC supports mechanisms that enable one to orient oneself within the broader spatial environment and to direct one’s movement towards navigational targets that are not currently visible. Interestingly, this division concords well with recent results from cognitive psychology, which indicate that spatial coding can use two different kinds of representation: viewpoint-specific scene snapshots and world-centered representations of spatial locations [89]. Because both PPA and RSC respond strongly during passive observation of navigationally relevant visual stimuli (i.e. scenes), these regions might be conceptualized as supporting distinct processing streams for visually guided navigation, both of which provide crucial inputs to the entorhinal cortex and the hippocampus.

Although speculative, I hypothesize that these input streams might be optimized for two different navigational situations. When we are lost and need to re-establish our general location, scene recognition mechanisms in the PPA are likely to be crucial, potentially enabling the correct ‘map’ to be selected in the hippocampus. Furthermore, when traveling through an unfamiliar environment, scene representations in the PPA might provide the building blocks out of which a larger topographical representation can be formed. Orientation mechanisms in RSC, however, might come into play once we know approximately where we are, by enabling us to specify directions to navigational goals [67]. These two processing streams would work in concert with several other neural mechanisms not described here, such as path integration mechanisms [90–92] and mechanisms for establishing head direction by reference to distal landmarks [2,93]. Future studies should relate these mechanisms more closely to spatial codes delineated by cognitive psychology and explore how

Box 3. Outstanding questions

- What is ‘spatial layout’ and how might it be encoded at the neural level? In particular, do neurons in the PPA respond selectively to different visual features (e.g. textures and colors), different environmental shapes (e.g. opening to the left and barrier to the right versus barrier to the left and opening to the right) or different spatial relationships between the observer and the environment (e.g. current heading is a 30° offset from the principal axis of the local environment)?
- Janzen and colleagues [27] report that a posterior parahippocampal region corresponding to the PPA responds more strongly to objects that were previously encountered at intersections than to equivalent objects that were previously encountered in non-navigationally relevant positions. What accounts for this ‘landmark object’ effect? Does it indicate that the PPA encodes the appearance of the landmark objects, the locations of the objects or the local spatial framework associated with each object?
- The location and boundaries of the PPA are well-described in the literature, but RSC is comparatively less studied. Does RSC operate as a unified functional unit or is it an agglomeration of more anatomically restricted components? If the former, what are its anatomical boundaries? If the latter, what are the distinct functions of the RSC subcomponents (retrosplenial cortex, posterior cingulate and parietal occipital sulcus)?
- Retrosplenial activity is often observed during episodic and autobiographical memory tasks that do not have an obviously spatial component [113]. Does this indicate that these kinds of memory involve an intrinsically spatial component such as ‘scene construction’ [114]? Or, does this indicate that the ‘true’ function of RSC should be described in more general terms that could potentially include processing of both spatial and nonspatial information?
- Results from neuroimaging and animal lesion studies indicate that navigation along highly familiar routes involves different memory systems than navigation along a novel route [115]. In particular, planning a novel route seems to involve hippocampal spatial representations, whereas navigation along a ‘well-worn’ route might use a response-based strategy that depends more on the basal ganglia (specifically, the caudate nucleus) [116,117]. Do the PPA and RSC have a role in response-based navigation? In particular, might the PPA encode crucial landmarks that prompt people to ‘turn left’ at a certain point [118]? And how might the information that it is important to ‘turn left here’ be differently encoded in the caudate nucleus versus RSC?

they might support both spatial and nonspatial memory (Box 3).

Acknowledgements

Supported by NIH grant EY-016464.

References

- 1 O’Keefe, J. and Nadel, L. (1978) *The Hippocampus as a Cognitive Map*. Clarendon Press; Oxford University Press
- 2 Taube, J.S. (1998) Head direction cells and the neurophysiological basis for a sense of direction. *Prog. Neurobiol.* 55, 225–256
- 3 Hafting, T. *et al.* (2005) Microstructure of a spatial map in the entorhinal cortex. *Nature* 436, 801–806
- 4 Maguire, E.A. *et al.* (1998) Knowing where and getting there: a human navigation network. *Science* 280, 921–924
- 5 Ghaem, O. *et al.* (1997) Mental navigation along memorized routes activates the hippocampus, precuneus, and insula. *Neuroreport* 8, 739–744
- 6 Rosenbaum, R.S. *et al.* (2004) I have often walked down this street before”: fMRI studies on the hippocampus and other structures during mental navigation of an old environment. *Hippocampus* 14, 826–835
- 7 Maguire, E.A. *et al.* (1997) Recalling routes around London: activation of the right hippocampus in taxi drivers. *J. Neurosci.* 17, 7103–7110

- 8 Ino, T. *et al.* (2002) Mental navigation in humans is processed in the anterior bank of the parieto-occipital sulcus. *Neurosci. Lett.* 322, 182–186
- 9 Rauchs, G. *et al.* (2008) Partially segregated neural networks for spatial and contextual memory in virtual navigation. *Hippocampus* 18, 503–518
- 10 Spiers, H.J. and Maguire, E.A. (2006) Thoughts, behaviour, and brain dynamics during navigation in the real world. *Neuroimage* 31, 1826–1840
- 11 Epstein, R. and Kanwisher, N. (1998) A cortical representation of the local visual environment. *Nature* 392, 598–601
- 12 Nakamura, K. *et al.* (2000) Functional delineation of the human occipito-temporal areas related to face and scene processing - A PET study. *Brain* 123, 1903–1912
- 13 Hasson, U. *et al.* (2003) Large-scale mirror-symmetry organization of human occipito-temporal object areas. *Neuron* 37, 1027–1041
- 14 Aguirre, G.K. *et al.* (1998) An area within human ventral cortex sensitive to “building” stimuli: evidence and implications. *Neuron* 21, 373–383
- 15 Aguirre, G.K. and D’Esposito, M. (1999) Topographical disorientation: a synthesis and taxonomy. *Brain* 122, 1613–1628
- 16 Bird, C.M. and Burgess, N. (2008) The hippocampus and memory: insights from spatial processing. *Nat. Rev. Neurosci.* 9, 182–194
- 17 Spiers, H.J. and Maguire, E.A. (2007) The neuroscience of remote spatial memory: a tale of two cities. *Neuroscience* 149, 7–27
- 18 Burgess, N. (2008) Spatial cognition and the brain. *Ann. N. Y. Acad. Sci.* 1124, 77–97
- 19 Downing, P.E. *et al.* (2006) Domain specificity in visual cortex. *Cereb. Cortex* 16, 1453–1461
- 20 Epstein, R. *et al.* (2003) Viewpoint-specific scene representations in human parahippocampal cortex. *Neuron* 37, 865–876
- 21 Epstein, R. *et al.* (1999) The parahippocampal place area: recognition, navigation, or encoding? *Neuron* 23, 115–125
- 22 Ishai, A. *et al.* (1999) Distributed representation of objects in the human ventral visual pathway. *Proc. Natl. Acad. Sci. U. S. A.* 96, 9379–9384
- 23 Epstein, R.A. *et al.* (2007) Visual scene processing in familiar and unfamiliar environments. *J. Neurophysiol.* 97, 3670–3683
- 24 Epstein, R.A. *et al.* (2007) Where am I now? Distinct roles for parahippocampal and retrosplenial cortices in place recognition. *J. Neurosci.* 27, 6141–6149
- 25 O’Craven, K.M. and Kanwisher, N. (2000) Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *J. Cogn. Neurosci.* 12, 1013–1023
- 26 Bar, M. and Aminoff, E. (2003) Cortical analysis of visual context. *Neuron* 38, 347–358
- 27 Janzen, G. and van Turenout, M. (2004) Selective neural representation of objects relevant for navigation. *Nat. Neurosci.* 7, 673–677
- 28 Epstein, R.A. (2005) The cortical basis of visual scene processing. *Vis. Cogn.* 12, 954–978
- 29 Saleem, K.S. *et al.* (2007) Cytoarchitectonic and chemoarchitectonic subdivisions of the perirhinal and parahippocampal cortices in macaque monkeys. *J. Comp. Neurol.* 500, 973–1006
- 30 Barrash, J. *et al.* (2000) The neuroanatomical correlates of route learning impairment. *Neuropsychologia* 38, 820–836
- 31 Pallis, C.A. (1955) Impaired identification of faces and places with agnosia for colours – report of a case due to cerebral embolism. *J. Neurol. Neurosurg. Psychiatry* 18, 218–224
- 32 Landis, T. *et al.* (1986) Loss of topographic familiarity. An environmental agnosia. *Arch. Neurol.* 43, 132–136
- 33 Mendez, M.F. and Cherrier, M.M. (2003) Agnosia for scenes in topographagnosia. *Neuropsychologia* 41, 1387–1395
- 34 Takahashi, N. and Kawamura, M. (2002) Pure topographical disorientation—the anatomical basis of landmark agnosia. *Cortex* 38, 717–725
- 35 Habib, M. and Sirigu, A. (1987) Pure topographical disorientation – a definition and anatomical basis. *Cortex* 23, 73–85
- 36 Epstein, R. *et al.* (2001) Neuropsychological evidence for a topographical learning mechanism in parahippocampal cortex. *Cogn. Neuropsychol.* 18, 481–508
- 37 Hecaen, H. *et al.* (1980) Loss of topographic memory with learning deficits. *Cortex* 16, 525–542
- 38 Steeves, J.K. *et al.* (2004) Behavioral and neuroimaging evidence for a contribution of color and texture information to scene classification in a patient with visual form agnosia. *J. Cogn. Neurosci.* 16, 955–965
- 39 Kim, M. *et al.* (2006) Anatomical correlates of the functional organization in the human occipitotemporal cortex. *Magn. Reson. Imaging* 24, 583–590
- 40 Lee, A.C.H. *et al.* (2005) Specialization in the medial temporal lobe for processing of objects and scenes. *Hippocampus* 15, 782–797
- 41 King, J.A. *et al.* (2002) The human hippocampus and viewpoint dependence in spatial memory. *Hippocampus* 12, 811–820
- 42 Hartley, T. *et al.* (2007) The hippocampus is required for short-term topographical memory in humans. *Hippocampus* 17, 34–48
- 43 Hassabis, D. *et al.* (2007) Patients with hippocampal amnesia cannot imagine new experiences. *Proc. Natl. Acad. Sci. U. S. A.* 104, 1726–1731
- 44 Summerfield, J.J. *et al.* (2006) Orienting attention based on long-term memory experience. *Neuron* 49, 905–916
- 45 Henderson, J.M. *et al.* (2008) Full scenes produce more activation than close-up scenes and scene-diagnostic objects in parahippocampal and retrosplenial cortex: an fMRI study. *Brain Cogn.* 66, 40–49
- 46 Shelton, A.L. and Pippitt, H.A. (2007) Fixed versus dynamic orientations in environmental learning from ground-level and aerial perspectives. *Psychol. Res.* 71, 333–346
- 47 Oliva, A. and Torralba, A. (2006) Building the gist of a scene: the role of global image features in recognition. *Prog. Brain Res.* 155, 23–36
- 48 Cheng, K. and Newcombe, N.S. (2005) Is there a geometric module for spatial orientation? Squaring theory and evidence. *Psychon. Bull. Rev.* 12, 1–23
- 49 Gallistel, C.R. (1990) *The Organization of Learning*. MIT Press
- 50 Cant, J.S. and Goodale, M.A. (2007) Attention to form or surface properties modulates different regions of human occipitotemporal cortex. *Cereb. Cortex* 17, 713–731
- 51 Vogt, B.A. *et al.* (2001) Cytology of human caudomedial cingulate, retrosplenial, and caudal parahippocampal cortices. *J. Comp. Neurol.* 438, 353–376
- 52 Kobayashi, Y. and Amaral, D.G. (2003) Macaque monkey retrosplenial cortex: II. Cortical afferents. *J. Comp. Neurol.* 466, 48–79
- 53 Kobayashi, Y. and Amaral, D.G. (2000) Macaque monkey retrosplenial cortex: I. three-dimensional and cytoarchitectonic organization. *J. Comp. Neurol.* 426, 339–365
- 54 Vogt, B.A. *et al.* (2005) Architecture and neurocytology of monkey cingulate gyrus. *J. Comp. Neurol.* 485, 218–239
- 55 Morris, R. *et al.* (1999) Architecture and connections of retrosplenial area 30 in the rhesus monkey (*Macaca mulatta*). *Eur. J. Neurosci.* 11, 2506–2518
- 56 Morris, R. *et al.* (2000) Architectonic analysis of the human retrosplenial cortex. *J. Comp. Neurol.* 421, 14–28
- 57 Sugiura, M. *et al.* (2005) Cortical representations of personally familiar objects and places: functional organization of the human posterior cingulate cortex. *J. Cogn. Neurosci.* 17, 183–198
- 58 Wolbers, T. and Buchel, C. (2005) Dissociable retrosplenial and hippocampal contributions to successful formation of survey representations. *J. Neurosci.* 25, 3333–3340
- 59 Vann, S.D. *et al.* (2000) Fos expression in the rostral thalamic nuclei and associated cortical regions in response to different spatial memory tests. *Neuroscience* 101, 983–991
- 60 Raichle, M.E. *et al.* (2001) A default mode of brain function. *Proc. Natl. Acad. Sci. U. S. A.* 98, 676–682
- 61 Kobayashi, Y. and Amaral, D.G. (2007) Macaque monkey retrosplenial cortex: III. Cortical efferents. *J. Comp. Neurol.* 502, 810–833
- 62 Insausti, R. *et al.* (1987) The entorhinal cortex of the monkey: II. Cortical afferents. *J. Comp. Neurol.* 264, 356–395
- 63 Suzuki, W.A. and Amaral, D.G. (1994) Perirhinal and parahippocampal cortices of the Macaque monkey – cortical afferents. *J. Comp. Neurol.* 350, 497–533
- 64 Vogt, B.A. *et al.* (1992) Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. *Cereb. Cortex* 2, 435–443
- 65 Maguire, E.A. (2001) The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. *Scand. J. Psychol.* 42, 225–238

- 66 Vogt, B.A. *et al.* (1987) Cingulate cortex of the rhesus monkey: I. Cytoarchitecture and thalamic afferents. *J. Comp. Neurol.* 262, 256–270
- 67 Byrne, P. *et al.* (2007) Remembering the past and imagining the future: a neural model of spatial memory and imagery. *Psychol. Rev.* 114, 340–375
- 68 Wyss, J.M. and Van Groen, T. (1992) Connections between the retrosplenial cortex and the hippocampal formation in the rat: a review. *Hippocampus* 2, 1–11
- 69 Furtak, S.C. *et al.* (2007) Functional neuroanatomy of the parahippocampal region in the rat: the perirhinal and postrhinal cortices. *Hippocampus* 17, 709–722
- 70 Takahashi, N. *et al.* (1997) Pure topographic disorientation due to right retrosplenial lesion. *Neurology* 49, 464–469
- 71 Ino, T. *et al.* (2007) Directional disorientation following left retrosplenial hemorrhage: a case report with fMRI studies. *Cortex* 43, 248–254
- 72 Katayama, K. *et al.* (1999) Pure topographical disorientation due to right posterior cingulate lesion. *Cortex* 35, 279–282
- 73 Bottini, G. *et al.* (1990) Topographic disorientation—a case report. *Neuropsychologia* 28, 309–312
- 74 Suzuki, K. *et al.* (1998) Pure topographical disorientation related to dysfunction of the viewpoint dependent visual system. *Cortex* 34, 589–599
- 75 Alsaadi, T. *et al.* (2000) Pure topographic disorientation: a distinctive syndrome with varied localization. *Neurology* 54, 1864–1866
- 76 Greene, K.K. *et al.* (2006) Topographical heading disorientation: a case study. *Appl. Neuropsychol.* 13, 269–274
- 77 Osawa, A. *et al.* (2008) Topographic disorientation and amnesia due to cerebral hemorrhage in the left retrosplenial region. *Eur. Neurol.* 59, 79–82
- 78 Aggleton, J.P. and Vann, S.D. (2004) Testing the importance of the retrosplenial navigation system: lesion size but not strain matters: a reply to Harker and Whishaw. *Neurosci. Biobehav. Rev.* 28, 525–531
- 79 Chen, L.L. *et al.* (1994) Head-direction cells in the rat posterior cortex. I. Anatomical distribution and behavioral modulation. *Exp. Brain Res.* 101, 8–23
- 80 Cho, J. and Sharp, P.E. (2001) Head direction, place, and movement correlates for cells in the rat retrosplenial cortex. *Behav. Neurosci.* 115, 3–25
- 81 Sato, N. *et al.* (2006) Navigation-associated medial parietal neurons in monkeys. *Proc. Natl. Acad. Sci. U. S. A.* 103, 17001–17006
- 82 Dean, H.L. and Platt, M.L. (2006) Allocentric spatial referencing of neuronal activity in macaque posterior cingulate cortex. *J. Neurosci.* 26, 1117–1127
- 83 Teng, E. and Squire, L.R. (1999) Memory for places learned long ago is intact after hippocampal damage. *Nature* 400, 675–677
- 84 Rosenbaum, R.S. *et al.* (2000) Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nat. Neurosci.* 3, 1044–1048
- 85 Rosenbaum, R.S. *et al.* (2007) Memory for familiar environments learned in the remote past: fMRI studies of healthy people and an amnesic person with extensive bilateral hippocampal lesions. *Hippocampus* 17, 1241–1251
- 86 Trullier, O. *et al.* (1997) Biologically based artificial navigation systems: review and prospects. *Prog. Neurobiol.* 51, 483–544
- 87 Kuipers, B. *et al.* (2003) The skeleton in the cognitive map – a computational and empirical exploration. *Environ. Behav.* 35, 81–106
- 88 Maguire, E.A. *et al.* (2006) Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain* 129, 2894–2907
- 89 Valiquette, C. and McNamara, T.P. (2007) Different mental representations for place recognition and goal localization. *Psychon. Bull. Rev.* 14, 676–680
- 90 Burgess, N. *et al.* (2007) An oscillatory interference model of grid cell firing. *Hippocampus* 17, 801–812
- 91 McNaughton, B.L. *et al.* (2006) Path integration and the neural basis of the ‘cognitive map’. *Nat. Rev. Neurosci.* 7, 663–678
- 92 Wolbers, T. *et al.* (2007) Differential recruitment of the hippocampus, medial prefrontal cortex, and the human motion complex during path integration in humans. *J. Neurosci.* 27, 9408–9416
- 93 Zugaro, M.B. *et al.* (2001) Background, but not foreground, spatial cues are taken as references for head direction responses by rat anterodorsal thalamus neurons. *J. Neurosci.* 21, RC154:1–5
- 94 Buffalo, E.A. *et al.* (2006) Distinct roles for medial temporal lobe structures in memory for objects and their locations. *Learn. Mem.* 13, 638–643
- 95 Suzuki, W.A. (1996) Neuroanatomy of the monkey entorhinal, perirhinal and parahippocampal cortices: organization of cortical inputs and interconnections with amygdala and striatum. *Semin. Neurosci.* 8, 3–12
- 96 Mort, D.J. *et al.* (2003) The anatomy of visual neglect. *Brain* 126, 1986–1997
- 97 Weniger, G. and Irle, E. (2006) Posterior parahippocampal gyrus lesions in the human impair egocentric learning in a virtual environment. *Eur. J. Neurosci.* 24, 2406–2414
- 98 Bohbot, V.D. *et al.* (1998) Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia* 36, 1217–1238
- 99 Bohbot, V.D. and Corkin, S. (2007) Posterior parahippocampal place learning in H.M. *Hippocampus* 17, 863–872
- 100 Ploner, C.J. *et al.* (2000) Lesions affecting the parahippocampal cortex yield spatial memory deficits in humans. *Cereb. Cortex* 10, 1211–1216
- 101 Epstein, R.A. *et al.* (2005) Learning places from views: variation in scene processing as a function of experience and navigational ability. *J. Cogn. Neurosci.* 17, 73–83
- 102 Epstein, R.A. *et al.* (2008) Two kinds of fMRI repetition suppression? Evidence for dissociable mechanisms. *J. Neurophysiol.* 99, 2877–2886
- 103 Ewbank, M.P. *et al.* (2005) fMR-adaptation reveals a distributed representation of inanimate objects and places in human visual cortex. *Neuroimage* 28, 268–279
- 104 MacEvoy, S.P. and Epstein, R.A. (2007) Position selectivity in scene- and object-responsive occipitotemporal regions. *J. Neurophysiol.* 98, 2089–2098
- 105 Park, S. *et al.* (2007) Beyond the edges of a view: boundary extension in human scene-selective visual cortex. *Neuron* 54, 335–342
- 106 Quiroga, R.Q. *et al.* (2005) Invariant visual representation by single neurons in the human brain. *Nature* 435, 1102–1107
- 107 Danckert, S.L. *et al.* (2007) Perirhinal and hippocampal contributions to visual recognition memory can be distinguished from those of occipito-temporal structures based on conscious awareness of prior occurrence. *Hippocampus* 17, 1081–1092
- 108 Yassa, M.A. and Stark, C.E. (2008) Multiple signals of recognition memory in the medial temporal lobe. *Hippocampus*, DOI: 10.1002/hipo.20452
- 109 Goh, J.O.S. *et al.* (2004) Cortical areas involved in object, background, and object-background processing revealed with functional magnetic resonance adaptation. *J. Neurosci.* 24, 10223–10228
- 110 Preston, A.R. and Gabrieli, J.D. (2008) Dissociation between Explicit Memory and Configural Memory in the Human Medial Temporal Lobe. *Cereb Cortex*, DOI: 10.1093/cercor/bhm245
- 111 Bakker, A. *et al.* (2008) Pattern separation in the human hippocampal CA3 and dentate gyrus. *Science* 319, 1640–1642
- 112 Xu, Y. *et al.* (2007) Dissociating task performance from fMRI repetition attenuation in ventral visual cortex. *J. Neurosci.* 27, 5981–5985
- 113 Svoboda, E. *et al.* (2006) The functional neuroanatomy of autobiographical memory: a meta-analysis. *Neuropsychologia* 44, 2189–2208
- 114 Hassabis, D. *et al.* (2007) Using imagination to understand the neural basis of episodic memory. *J. Neurosci.* 27, 14365–14374
- 115 Iaria, G. *et al.* (2003) Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *J. Neurosci.* 23, 5945–5952
- 116 Packard, M.G. and McGaugh, J.L. (1996) Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. *Neurobiol. Learn. Mem.* 65, 65–72
- 117 Hartley, T. *et al.* (2003) The well-worn route and the path less traveled: distinct neural bases of route following and wayfinding in humans. *Neuron* 37, 877–888
- 118 Janzen, G. and Weststeijn, C.G. (2007) Neural representation of object location and route direction: an event-related fMRI study. *Brain Res.* 1165, 116–125