The Anatomy and Function of the Postrhinal Cortex

Review

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Abstract (250 words)

The parahippocampal cortex in the primate brain is implicated in the medial temporal lobe memory network for spatial and episodic memory, but the precise function of this region remains unclear. Importantly, the rodent postrhinal cortex provides a structural and connectional homolog to the primate parahippocampal cortex. This homology permits the use of the powerful tools available in rodent models to better understand the function of the parahippocampal cortex in the human and non-human primate brains. Although many articles have compared and dissociated the function of the rodent POR from other areas in the medial temporal lobe implicated in learning, memory, and memory-guided behavior, there are no in-depth reviews, particularly covering the last two decades of research. Nor has there been a review of the literature on the potential role of the POR in attention. Here, we review the anatomical and functional connectivity of the postrhinal cortex in rats, examine the evidence for proposed behavioral functions of this region, and suggest a model that accounts for the array of observations. We propose that the rodent POR binds non-spatial information and spatial information to represent the current local physical environment or context, including the geometry of the space and the spatial layout of objects and features in the environment. The POR also automatically monitors the environment for changes and updates representations when changes occur. These representations of context are available to be used by multiple brain regions, including prefrontal, posterior cortical, and hippocampal areas, for context-guided behavior, associative learning, and episodic memory.

Keywords: context, scene, navigation, associative learning, conjunctive coding

The medial temporal lobe (MTL) is implicated in episodic memory, associative learning, and spatial learning. Based on lesion studies utilizing extensive behavioral tests combined with anatomical studies, the regions in the MTL are well identified and, to a certain extent, functionally dissociated. Since its initial anatomical and connectional dissociation from the rodent perirhinal cortex, the postrhinal cortex (POR) is understood to be a key component in the MTL memory system (Burwell et al., 1995; Deacon et al., 1983; Beaudin et al., 2013). Yet, its specific function remains unclear. Previous reviews focused on differentiating the POR from other regions in the MTL, for example, the hippocampus and perirhinal cortex (Aggleton et al., 2012), the entorhinal cortices (Eichenbaum et al., 2007), and the retrosplenial cortex (Bucci & Robinson, 2014). None of these proposals of POR function, however, account for all available observations. Here, we review the evidence from anatomical and functional studies of the rat POR and propose a unified theory of how the POR contributes to memory and other cognitive processes.

Anatomy of the POR

Location and Structure

The POR is located near the caudal pole of the rodent brain (Burwell, 2001; Beaudin et al., 2013). It is bordered rostrally by the perirhinal cortex (PER, Figure 1A, D). What we now call the POR was originally the caudal part of the PER. This area was parceled out and defined as the POR on the basis of cytoarchitectonic, connectional, topographical, and functional criteria, particularly the similarity of corticocortical connectivity with the primate parahippocampal cortex (Burwell, Witter, and Amaral, 1995). The POR is bordered dorsally by visual association cortex, ventrally by the medial entorhinal cortex, and medially by agranular retrosplenial cortex at its most caudal extent (Vogt & Miller, 1983). Interestingly, in both rodents and primates, the parasubiculum inserts itself between the POR and MEC (Figure 1D-E).

Cytoarchitecturally, the POR can be identified by the presence of ectopic layer II cells in layer I at the region's border with the PER and MEC (Figure 2). A more densely packed layer II as compared to that of the PER further defines the POR, as does its deep layers, which contain elongated cells oriented radially as compared to the elongated cells oriented horizontally in the PER.

Three main cell types have been recorded in the POR, including two major inhibitory classes and a single, functionally restricted class of pyramidal cells (Sills et al., 2012). Fast-spiking cells, composed entirely of multipolar nonpyramidal cells, and low threshold-spiking cells, composed mainly of multipolar and bitufted dendrites make up the two inhibitory classes of cells found in the POR. Interestingly, there is a specific lack of parvalbumin expressing fast-spiking cells in the ventral portion of the POR, distinguishing it from surrounding cortical regions (Sugden, 2008; Beaudin et al., 2013; de Curtis and Paré, 2004). The more homogenous pyramidal cells make up the third class, the regular-spiking cells (Sills et al., 2012). Interestingly, no intrinsically bursting pyramidal neurons were seen in the POR, which is similar to what is seen in the entorhinal cortices, but specifically different from what is seen in the PER.

Connections

A schematic of the major connections of the POR is shown in Figure 3. In this section, we consider the connections with other neocortical regions, other parahippocampal region structures and the structures in the hippocampal formation, and finally subcortical areas. The parahippocampal region comprises the perirhinal cortex (PER), the POR, the lateral and medial entorhinal cortices (LEC and MEC), and the pre- and para-subiculum. The hippocampal formation comprises the dentate gyrus, CA3, CA2, CA1, and the subiculum.

Neocortical connections

The POR is more heavily connected with caudal neocortical regions than rostral ones. More specifically, POR is robustly and reciprocally connected with the dorsal retrosplenial, posterior parietal, and ventral temporal area. It also has strong reciprocal connections with lateral and medial visual association cortex. There is even a smaller reciprocal connection with primary visual cortex.

Approximately two-thirds of POR afferents come from neocortical regions, with a large portion of these originating in these visuospatial and visual association areas. The POR is heavily and reciprocally connected with the posterior parietal cortex, ventral temporal association areas, and retrosplenial cortex (Agster & Burwell, 2009; Burwell & Amaral, 1998b). The posterior parietal cortex is known to be important in movement planning, spatial reasoning, and attention. Ventral temporal association areas, which receive projections from motion detection regions and object recognition regions, are thought to be involved in the interpretation of dynamic moving objects. The retrosplenial projection provides moderate input to the dorsal retrosplenial area and light input to the ventral retrosplenial area. The retrosplenial cortex, especially the dorsal retrosplenial cortex, is known to be important for using surrounding visual cues to accomplish tasks. The POR is also connected with frontal and prefrontal areas though the strength of these connections varies across frontal regions. The POR also strongly projects to the posterior parietal cortex, with caudal regions of the POR projecting more strongly than rostral regions. POR projections to the piriform and insular cortices are minimal. Although there is some input from auditory association cortex, the POR mainly receives visual and visuospatial information from the cortical regions.

The POR is reciprocally connected a number of frontal regions, but the strongest connections are with the secondary motor cortex (MOs, also called the medial precentral cortex, medial agranular cortex, dorsomedial prefrontal cortex, second frontal area, and frontal orienting field) followed by the orbitofrontal cortex (Agster & Burwell, 2009; Burwell & Amaral, 1998b; Delatour & Witter, 2002; Hwang et al., 2018), The MOs is proposed to be the rodent homolog of the primate dorsolateral prefrontal cortex (Hwang et al., 2018; Uylings et al., 2003).

Parahippocampal Connections

The majority of parahippocampal inputs to the POR come from the PER and the entorhinal cortex (Burwell & Amaral, 1998a; Scaplen et al., 2017). The POR projects most strongly to the caudal PER, but it does project to the entire rostrocaudal extent. The POR provides a widespread project to the medial entorhinal cortex, but it also projects to the caudal aspect of the lateral entorhinal cortex (Burwell & Amaral, 1998a; Naber et al., 1997; LEC). These efferents are made up mainly of excitatory projections, which suggests the potential for efficient high-volume information transfer (Koganezawa et al., 2015). For both projections to the entorhinal areas, the POR projects mainly to the lateral band, which in turn projects to the dorsal hippocampus. Likewise, the POR projects most strongly to the medial entorhinal cortex (MEC), but also to the caudal LEC. Of the other parahippocampal structures, the POR projects strongly to caudal parasubiculum as well as the dorsal presubiculum, sometimes also called postsubiculum (Agster & Burwell, 2013).

The parahippocampal efferents and afferents are largely reciprocal. The POR projects most strongly to the PER and the entorhinal cortex (Burwell & Amaral, 1998a). The POR primarily targets caudal PER, but it targets the entire rostrocaudal extent of the PER. POR projects most strongly to the MEC and the caudal LEC. The POR projects strongly to caudal parasubiculum and to dorsal presubiculum (Agster & Burwell, 2013).

Hippocampal Formation Connections

The majority of hippocampal inputs to the POR come from the presubiculum, particularly the dorsal presubiculum (Agster & Burwell, 2013). These afferents account for approximately seventy percent of the total hippocampal input to POR. Contribution from hippocampus proper to the POR comes almost entirely from dorsal CA1, with a small portion of afferents coming from ventral CA1. There is very little input from CA2 or CA3 to POR and little or no direct input from the dentate gyrus. Interestingly, dorsal hippocampus provides substantially more output to the POR than to the other parahippocampal areas such as the perirhinal or entorhinal cortices (Agster & Burwell, 2013).

Just as the majority of hippocampal inputs to the POR were from subicular regions, a majority of the POR outputs to the hippocampus are also to the subicular areas. The POR projects strongest to the caudal parasubiculum, followed closely by the dorsal subiculum and presubiculum. POR projects moderately to both dorsal and ventral CA1, and dorsal dentate gyrus. Projections from the POR to dorsal and ventral CA2 and ventral subiculum are very weak, with little to no projections to dorsal and ventral CA3 or ventral dentate gyrus (Agster & Burwell, 2013).

Subcortical Connections

The subcortical connections to the POR are relatively weak as compared with corticortical connections. It should be noted, however, that subcortical structures are often smaller. Thus, classic neuroanatomical techniques which rely on densities of labeled fibers and numbers of labeled cells may not represent the functional importance of smaller subcortical projections. That said, connections with dorsal thalamic group and the claustrum are quite strong. The largest subcortical input to the POR comes from the laterodorsal and lateral posterior areas of the thalamus, with these connections accounting for approximately two fifths of the total subcortical input to the POR (Tomás Pereira et al., 2016). The lateral posterior nucleus (LPn) provides the strongest thalamic connections with the POR, but there is also a small input from the lateral geniculate nucleus. The LPn is the putative homolog of the pulvinar in the primate brain (Baldwin et al., 2017; Kaas & Baldwin, 2019). There is also evidence for connectivity with the superior colliculus (Beltramo, 2020; Beltramo & Scanziani, 2019). These areas are known to be involved in visual association, visual integration, and spatial cognition. Interestingly, the POR also receives a strong input from the claustrum, which accounts for about one fifth of the subcortical input to the POR. The claustrum core has widespread reciprocal connections with neocortical areas and also receives input from subcortical structures. One proposed function is that the claustrum contributes to multisensory integration (Mathur, 2014). Notably, the claustrum has a dedicated visual zone, but it is not known whether the POR is preferentially connected with this zone.

The lateral and basolateral nuclei of the amygdala provide moderate inputs to the POR as well. These amygdalar nuclei are known to be important in processing affective information. One group working in mice defined separate muscarinic acetylcholine receptor 2 (M2)-positive or M2-negative modules in the POR. (Meier et al., 2021). The M2- module one is preferentially connected with the amygdala and projects to the entorhinal cortex. The other module receives inputs from the visual thalamus, the lateral geniculate, and the pulvinar.

Other subcortical inputs include a moderate projection from medial septum, a nucleus that serves an important role in modulating theta activity in the hippocampus via inhibitory pacemaking. The hypothalamus also has weak projections to the POR, primarily from the mamillary bodies and the lateral zone, regions implicated in memory. In contrast, the basal ganglia and the olfactory regions provide little to no input to the POR (Tomás Pereira et al., 2016).

Despite the extremely weak input from the basal ganglia to the POR, the output from the POR to the basal ganglia, specifically the caudoputamen, makes up about one third of the subcortical output from the POR. The dorsal striatum is important in movement planning, and especially in the learning of habitual behavior (Kroemer et al., 2016). The POR also strongly innervates both the dorsal and ventral thalamic groups, with an especially strong reciprocal connection to the lateral posterior nucleus. The POR moderately innervates the amygdala, primarily targeting the lateral amygdala, basolateral amygdala, and central amygdala nuclei. Projections from POR to claustrum are relatively weak, compared to the amount of input received from the area as well as compared to the amount of input claustrum receives from other parahippocampal areas such as the perirhinal and entorhinal cortices. POR input to the septal nuclei is similarly weak, with minimal labeling exclusively in the lateral septal nuclei. Finally, the hypothalamus and olfactory regions had similarly weak input received from the POR (Agster et al., 2016).

Postrhinal Functions

Historically, the POR was understood as a gateway for neocortical visuospatial information to the hippocampus with the dorsal visual stream (the "where pathway") targeting the POR, and the ventral visual stream (the "what pathway") targeting the PER (Eacott et al., 1994; Squire et al., 2004). By this view, the perirhinal cortex projects object information to the lateral entorhinal cortex, which then passes it on to the hippocampus. On the other hand, the POR sends spatial information to the medial entorhinal cortex, which also passes it on to the hippocampus making up the "where" pathway extension. The hippocampus would then bind the object information and the spatial information for the purpose of episodic memory (Eichenbaum, 2000; Eichenbaum et al., 2007; Knierim et al., 2006). This view, however, understates the roles of the regions upstream of the hippocampus by presenting them as simple relay areas and overlooks the cross-talk between these two pathways at multiple levels (Figure 4), For example, the POR projects to both the lateral and medial entorhinal cortices (Burwell & Amaral, 1998a; Witter, 2010) as well as directly to the hippocampus (Agster & Burwell, 2013; Naber et al., 1997b; Naber et al., 2001). There are direct and reciprocal connections between the PER and the POR (Burwell & Amaral, 1998a) as well as direct connections from the PER and the POR to CA1/subiculum. (Naber et al., 1997). There are also substantial intrinsic connections across the lateral and medial entorhinal cortices (Chrobak & Amaral, 2007; Dolorfo & Amaral, 1998). Finally, it is clear that the upstream structures have functions independent of the hippocampus. Indeed, the POR has been shown to play an important role in many processing functions that extend well beyond relaying sensory information.

Attentional processes

One question that arises with regard to the medial temporal lobe memory system is how items to be remembered are identified for further processing. One possibility is that some medial temporal lobe structures also have attentional functions. Posner and colleagues proposed multiple systems for mediating attentional mechanisms (Posner & Petersen, 1990; Posner et al., 1998). The anterior, or detection, network is proposed to mediate “top-down” attention by enhancing the neural processing of sensory input, thus increasing the signal-to-noise ratio and facilitating attentional bias. In the human brain, the so-called anterior network involves anterior cingulate regions, posterior parietal regions, and the dorsolateral prefrontal cortex (Posner & Petersen, 1990). The POR is reciprocally connected with the MOs, the rodent homolog of the primate dorsolateral prefrontal cortex. MOs neurons encode choice actions during action planning and these choice signals occur earlier than in the primary motor cortex and other brain areas, suggesting it may be involved in decision-making processes (Peng & Burwell, 2021). Thus, the MOs may rely on the POR for contextual information when the outcome of action choices is modulated by context.

In contrast, the posterior, or orienting, network is proposed to mediate “bottom-up” attentional mechanisms that are driven by target salience and sensory context that in turn trigger attentional processing by higher cortical areas. The POR is heavily interconnected with the regions of the posterior network, including posterior parietal cortex, the pulvinar, and the superior colliculus. These connections combined with its other subcortical, cortical, and hippocampal connections position the POR to be an ideal region to aid in directing attention for memory. There is evidence to suggest that it does just that. For example, damage to the POR produced deficits in attentional orienting in a conditioned orienting task (Bucci & Burwell, 2004). Further, there is evidence that the POR modulates attention in response to changes in the environmental context. In a cue rotation paradigm, POR cells were shown to remap quickly and unpredictably following cue rotation, and did not return to their baseline firing maps when the cues were returned to their original positions, but rather remapped again (Burwell & Hafeman, 2003).

This suggests that POR cells are attending to changes in environmental context, and because of the position of the POR within different networks, this could in turn bias attention in higher cortical areas.

Spatial memory and navigation

The literature on the role of the POR in spatial memory and navigation is mixed. One issue is that, in earlier work, studies using experimental lesions sometimes lesioned both the PER and the POR. One study using combined cytotoxic lesions of the PER and POR reported deficits in spontaneous object recognition, but spared function of spatial working memory in a T-maze task (Aggleton et al., 1997). Similarly, combined *N*-methyl-D-aspartate (NMDA) lesions of the PER and POR disrupted object discrimination but spared performance on the Morris water maze task and standard radial arm maze task (Bussey et al., 1999). Further, rats with these combined lesions of the PER and POR were reported to outperform controls in a spatially guided T-maze task when the retention delay was increased to 60s (Bussey et al., 2000). These studies convergently suggest that whereas the PER and POR are important in object discrimination and retention, they are not necessary for spatial memory. Similarly, neurotoxic lesions that were focused on the POR were shown to cause deficits in contextual fear conditioning (Bucci et al., 2000) and contextual discrimination (Bucci et al., 2002), while having no impact on performance on the water maze (Burwell et al., 2004a). This group further reported that combined lesions of the PER, POR, and entorhinal cortices failed to impair place learning. One study reported that NMDA lesions centered on the POR produced deficits in reference memory and working memory versions of the Morris water maze task and the radial arm maze task as well in delay-nonmatching-to-place versions of the radial arm maze and T-maze. (Liu & Bilkey, 2002). These experiments were run using albino rats in low light conditions with distal cues located quite far from the mazes. A subsequent review of disparate impact of perirhinal lesions on spatial tasks revealed that in these studies, deficits could be accounted for by these strain differences and differences in methods (Aggleton et al., 2004). For example, pigmented rats with POR damage showed no impairments in the Morris water maze under conditions of high light and when distal cues were placed on the curtains surrounding the maze (Burwell et al., 2004b).

Scene perception, contextual learning and memory

One candidate for what the POR contribution is to spatial information processing is the representation of the environmental context. POR damage reliably causes deficits in contextual fear conditioning (Bucci et al., 2000) and contextual discrimination (Bucci et al., 2002). In the discrimination experiments, rats were trained to differentiate between two contexts, one of which was paired with a shock. Animals with sham lesions were able to differentiate between the two contexts by the third day of training, as shown by decreased freezing in the non-shock paired context, whereas animals with POR lesions tended to freeze more in both contexts, showing an inability to distinguish the two contexts. A similar conclusion can be drawn from subsequent studies showing that animals with POR lesions froze less across all contexts following successful fear conditioning training, with the result being a tendency for animals with POR lesions to overgeneralize rather than differentiate between contexts (Burwell et al., 2004; Peck & Taube, 2017). A series of lesion experiments also demonstrated the importance of the POR in contextual scene representation (Eacott & Gaffan, 2005; Gaffan et al., 2004; Norman & Eacott, 2005). In these experiments, rats with postrhinal lesions exhibited deficits in recognizing familiar objects in a new context, but recognition of the objects themselves was spared. Further, the POR neurons respond to changes in the spatial relationship between objects and their background context (Howard et al., 2011), providing evidence for an attentional function of the POR along with the representation of environmental context (Figure 5). Thus, in addition to representing the current environment context, the POR may be monitoring the current context in order to update the representation when changes occur.

Associations and conjunctions

Both allocentric and egocentric representations have been observed in the POR, as have cells that respond conjunctively to two or more different spatial representations within an environment (LaChance et al., 2019). In these experiments, neurons recorded from the POR were shown to encode three distinct aspects of the environment: “Center-bearing” cells encoded the egocentric bearing of the center of the arena; “center-distance” cells showed tuning to the animal’s distance to the center of the arena in both positive and negative linear responses; and head direction cells were observed, with these cells responding to the direction of the rat’s head in an allocentric reference frame. Unlike classic head direction cells, more than half (51%) of recorded cells that encoded one of these variables also showed conjunctive coding to at least one other spatial variable. These findings are consistent with the view that the POR represents context, in part, by encoding the spatial layout of objects and features in the local spatial context.

If the POR is important for encoding context, it should not be surprising to observe responses to both non-spatial visual information, such as objects and features of a scene or context, and spatial visual information, such as the spatial layout of such objects in a scene or physical space. Accordingly, the POR cells show responses via immediate-early gene activation to both spatial and non-spatial tasks at comparable levels (Beer et al., 2013). This group further suggested that the POR responded to both spatial and object information. POR cells also responded preferentially to an object when it was in a particular location, or object-location conjunction cells (Furtak et al., 2012).

Hippocampal cells also show such object-location conjunctive coding (Komorowski et al. 2009). These object location conjunctions, however, appeared as animals learned to associate the object in a particular location with a reward. In contrast, when recording simultaneously in the POR and the hippocampus, we showed that object-location conjunctions appear earlier in training in the POR compared with the hippocampus (Estela-Pro, 2021). Thus, object-location conjunctive coding appears in the POR before associative learning and conjunctive coding emerge in the hippocampus. This is consistent with the view that context is represented somewhat automatically in the POR. These representations are then available to the hippocampus for associative learning and episodic memory.

Neuronal oscillations in the POR

Brain oscillations as recorded in local field potentials (LFPs) are implicated in both sensory and cognitive processes. The most widely accepted band definitions in the rodent include delta (~0-4 Hz), theta (~4-12 Hz), beta (~13-30 Hz), and gamma (>30 Hz; Buzsaki & Draguhn, 2004). Oscillatory band definitions in humans are similar, except that in humans, theta is generally defined as 4-8 Hz and there is an alpha band defined at 8-12 Hz (Lever et al., 2014). Therefore, the theta frequency band in rodents is comparatively broad as the frequencies analogous to alpha in the human brain are instead included within the theta band. The theta rhythm is a large amplitude, relatively slow (4–12 Hz), and highly regular rhythm that has been shown to play an important role in navigation as well as spatial and episodic memory processing (Buzsaki, 2005). The rodent hippocampal network literature focuses primarily on two frequencies — theta and gamma. Two types of theta have been described: Type 1 theta (6-12 Hz) is positively correlated with running speed and is atropine resistant; Type 2 theta (4-9 Hz) is more closely associated with immobility and is blocked with the administration of atropine (Bland, 1986). The vast majority of studies of theta in rats focus on the hippocampal theta rhythm and its role in navigation and spatial memory, thus focusing predominantly on Type 1 movement-associated theta (6-12 Hz). Theta rhythms in the hippocampus correlate with theta in many cortical and subcortical hippocampal efferent and afferent structures, including the entorhinal cortex (Mitchell & Ranck Jr., 1980), medial septum (Nerad & McNaughton, 2006), amygdala (Seidenbecher et al., 2003), parasubiculum (Glasgow & Chapman, 2007), and prefrontal cortex (Jones & Wilson, 2005). Functionally, the theta rhythm in rodents has been shown to correlate with the intake of sensory information during exploratory movements such as whisking and sniffing, with each theta cycle serving as a mechanism to temporally segment the samples of stimuli from the environment (Kepecs et al., 2005). The second main rhythm studied in the HC, gamma oscillations, are thought to temporally link the activity of distributed cells both within and between regions (Colgin & Moser, 2010). These oscillations are relatively fast (>30 Hz), and unlike theta rhythms, which tend to remain relatively stable throughout active behaviors, gamma oscillations tend to occur in bursts at particular times within the theta cycle (Bragin et al., 1995; Colgin et al., 2009). Functionally, these high frequency gamma oscillations are thought to be ideally suited to coordinate operations on a time scale that is beyond the range of conscious perception, such as rapidly selecting inputs, grouping neurons into functional ensembles, and retrieving memories necessary to perform the current task (Colgin & Moser, 2010).

For the POR, only two studies have examined the occurrence or function of theta or gamma. The first study reported that theta power differed across task epochs, with theta power being higher during "task-relevant" epochs compared to "task-irrelevant epochs". In addition, theta power increased following incorrect trials compared to correct trials (Furtak et al., 2012). Both of these findings suggest an attentional function of theta, possibly as an error signal. Phase locking of cells to theta was also examined, and it was found that a proportion of cells (38% of recorded cells) were phase-locked to theta, with putative pyramidal cells typically being locked to the trough of theta and putative fast-spiking cells being locked mainly to the peak of theta (Furtak et al., 2012). This suggests theta is an important mechanism in the POR for information transfer, and the similarities between POR theta and HC theta suggest that it is likely an important information relay mechanism between the POR and other regions including the HC. Phase locking of cells with gamma was also examined in the referenced study, with large proportions of cells being phase locked to both low gamma and high gamma, although there were no task-related differences seen with respect to gamma power or phase-locking.

The second study examined the instantaneous amplitude and shape of theta oscillations in the POR as they relate to running speed (Ghosh et al., 2020). Theta in the POR was found to mimic theta in the HC in that it is temporally asymmetrical, with the falling phase of theta cycles lasting longer than the subsequent rising phase. These reported results suggest that the amplitude and waveform shape of individual theta cycles might be governed by partially independent mechanisms, highlighting the importance of examining single cycles in order to understand the behavioral correlates of cortical theta rhythms.

The role of the postrhinal cortex in the medial temporal lobe

Each region within the medial temporal area serves a specific and distinct role, including the POR. Many of these functions are informed by neuroanatomical connections (Figure 6). For example, the PER is known to be important for processing information about objects, items, and object features, and is in position to provide such information to the POR, the LEC, and the hippocampus. We propose that this object and item information is provided to the POR for representing objects and features in the local context, to the LEC for representing topological space and for egocentric processing, and to the hippocampus for associative learning and episodic memory. The POR receives visuospatial information from the PPC, the RSP, visual association regions, and we propose this information is also important for the spatial components of context representations. The PPC is involved in a variety of complex cognitive processes including attention, spatial awareness, navigation, and movement planning (Bucci, 2009; Colby and Goldberg, 1999; Corbetta and Shulman, 2002; Reep and Corwin, 2009; Kuang et al., 2015), whereas the RSC is thought to support mechanisms that allow a scene to be localized within the broader spatial environment (Epstein et al. 2007; Epstein, 2008). This network allows a complex representation of context that can then be provided to the MOs for context guided action choices.

The MEC is known to contain grid cells as well as speed cells, both of which directly contribute to the view that the MEC is important in the representation of geometric or Euclidean space (Hafting et al., 2005; Kropff et al., 2015). Conversely, the LEC has been implicated in the representation of time (Tsao et al., 2018) as well as the representation of egocentric space (Wang et al., 2018), lending to the view that the LEC is important in representing relative or topological space. The object information provided to the LEC by the PER also appears to be important for representing topological space and for hippocampal processing of objects and landmarks important for navigation (Scaplen et al., 2014; Scaplen et al., 2017). The hippocampus is widely acknowledged to be crucially involved in navigation (O'Keefe and Dostrovsky, 1971; Eichenbaum, 2017; van Kesteren et al., 2018) associative learning (Suzuki, 2007; Eichenbaum and Cohen, 2001; Squire and Zola, 1996; Wirth et al., 2003), and episodic memory (Tulving and Markowitsch, 1998; O'Keefe & Nadal, 1978; Eichenbaum, 2000; Smith and Mizumori, 2006; Arnold et al., 2018), The HC is often thought of as the principal processor of the medial temporal network, where item information is combined with spatial information. We have shown, however, that the POR also encodes combined item and spatial information in the form of conjunctive cell responses (Estela-Pro, 2021), which suggests that the POR serves a larger role within this network than originally thought (see Figure 6).

Based on the data reviewed above, we propose that the rodent POR represents the current physical environment, or context, including the geometry of the space and the spatial layout of objects and features in the environment. To do this, the POR integrates visual information received from primarily visual areas such as visual association cortex and superior colliculus, as well as processed information received from spatial and item processing regions such as posterior parietal cortex, retrosplenial cortex, lateral and medial entorhinal cortices, and perirhinal cortex. Further, the POR monitors the environment for changes and updates the current context representation accordingly and in an automatic manner. This process likely draws heavily on the POR's connections to attentional regions such as PPC, MOs, and pulvinar (Yang and Burwell, 2020; Figure 6). These context representations are then used by multiple brain regions for context guided behavior, for example by frontal regions for decision-making, by retrosplenial cortex for forming context frames, and by the hippocampus for associative learning and episodic memory.

How does our theory relate to prior views? Some prior theories of POR function have focused on differentiating the POR from other regions in the MTL. One view focused on differentiating the role of the perirhinal cortex from the hippocampus in novelty recognition and associative memory and suggested that the role of the POR was specific to recognition tasks that involve spatial or contextual information (Aggleton et al., 2012). These findings are consistent with our theory of POR function. Indeed, if the POR represents the spatial layout of objects in the current environment, then the POR would be involved in recognizing that a familiar object is being presented in a different location. By another view, Eichenbaum and colleagues described the segregated "what" and "where" pathways to the medial temporal lobe, suggesting that the POR is in the spatial pathway and that POR neurons encode spatial features of the environment as opposed to individual stimuli (Eichenbaum et al., 2007). Again, this is consistent with our view, but does not take into account the findings that the POR codes for objects and locations (Futak, Ahmed, and Burwell, 2012). Another view differentiates retrosplenial and postrhinal contributions to learning and memory, suggesting that the POR serves to detect behaviorally relevant changes in contextual stimuli and relay that new status specifically to RSC (Bucci & Robinson, 2014). Whereas we think the POR does relay contextual information to the RSC, our data provide evidence that the POR is automatically detecting changes to the context, even when such changes are not task-relevant (Burwell and Hafeman, 2003; Bucci and Burwell, 2004).

Thus, the POR the encoding and monitoring functions of the POR subserve attention, location, scene perception, and contextual learning. As such, the POR acts as an important part of the posterior attentional network to signal changes in the local environmental context, encoding these changes as conjunctions of the various aspects of the context. This includes conjunctions of allocentric and egocentric spatial orientation (LaChance et al., 2019) as well as conjunctive representations of the objects, patterns, and locations that together make up the local physical environment (Furtak et al., 2012, Estela-Pro, 2021).

The human homologue of the POR, the parahippocampal cortex (PHC), has been shown to process nonspatial information along with spatial information. Bar and Aminoff (2003) suggested that the PHC may be representing objects that have associations with particular kinds of contexts, for example stoves which are usually in kitchens, or particular categories of contexts, for example all kitchens. Bar and colleagues proposed that the PHC is mediating both spatial and non-spatial contextual associations particularly strong contextual associations rather than representing places, contexts, or scenes, themselves (Bar et al., 2008).

These ideas about PHC function are consistent with our proposal that the rodent POR represents the current physical environment, including the geometry of the space and the spatial layout of the items and patterns in the space. The POR automatically monitors the current environment for changes and updates the current context representation, accordingly, when changes occur. These representations are then used by other brain regions for context-guided behavior and cognition. What might be a novel prediction of our theory of POR function? If the POR automatically monitors context and updates the current representation, we should see object-location conjunctive coding resulting from updating context in the POR before we see object-location conjunctions resulting from associative learning in other brain regions. Indeed, we have made such an observation observation (Estela-Pro, 2021). As discussed earlier, hippocampal cells show object-location conjunctive coding which emerges as animals learn to associate a rewarded object with a place (Komorowski et al. 2009). When recording simultaneously in the POR and the hippocampus during discrimination learning, we observed object location conjunctive coding in the POR before it emerged in the hippocampus. This is consistent with the view that context is represented automatically in the POR and that such representations are available to other brain regions for context-guided behavior and cognition.

Conclusion

Here we review the cortical, subcortical, and hippocampal connectivity of the POR, as well as the numerous behavioral functions in which the POR has been implicated. Taken together, the behavioral evidence supports a view of postrhinal and parahippocampal function that is consistent with the anatomical and functional evidence (Figure 6). We suggest the POR combines object and feature information from the PER with spatial information from RSC, PPC, secondary visual cortex, and the pulvinar to represent the spatial layout of objects and features in specific environmental contexts. As well as maintaining a representation of the current context, the POR also has an attentional role in that it monitors the context for changes and updates that representation when changes occur. The representation is made available to other regions for the binding of events with context to form episodes that are located in time, for guiding context-relevant behavior, and for recognizing objects in scenes and contexts.

References

Aggleton, J., Kyd, R., & Bilkey, D. (2004). When is the perirhinal cortex necessary for the performance of spatial memory tasks? *Neuroscience & Biobehavioral Reviews*, *28*(6), 611–624. https://doi.org/10.1016/j.neubiorev.2004.08.007

Aggleton, J. P., Brown, M. W., & Albasser, M. M. (2012). Contrasting brain activity patterns for item recognition memory and associative recognition memory: Insights from immediate-early gene functional imaging. *Neuropsychologia*, *50*(13), 3141–3155. https://doi.org/10.1016/j.neuropsychologia.2012.05.018

Aggleton, J. P., Keen, S., Warburton, E. C., & Bussey, T. J. (1997). Extensive cytotoxic lesions involving both the rhinal cortices and area TE impair recognition but spare spatial alternation in the rat. *Brain Research Bulletin*, *43*(3), 279–287. https://doi.org/10.1016/s0361-9230(97)00007-5

Aggleton, J. P., Vann, S. D., Oswald, C. J., & Good, M. (2000). Identifying cortical inputs to the rat hippocampus that subserve allocentric spatial processes: A simple problem with a complex answer. *Hippocampus*, *10*(4), 466–474. https://doi.org/10.1002/1098-1063(2000)10:4<466::AID-HIPO13>3.0.CO;2-Y

Agster, K. L., & Burwell, R. D. (2008). Anatomy of the Hippocampus and the Declarative Memory System. In *H. E. Eichenbaum (Ed.), Sys and Neurosci: Vol. Vol. 3* (1st ed., pp. 47–66). Elsevier.

Agster, K. L., & Burwell, R. D. (2009). Cortical efferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. *Hippocampus*, *19*(12), 1159–1186. https://doi.org/10.1002/hipo.20578

Agster, K. L., & Burwell, R. D. (2013). Hippocampal and subicular efferents and afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. *Behavioural Brain Research*, *254*, 50–64. https://doi.org/10.1016/j.bbr.2013.07.005

Agster, K. L., Tomás Pereira, I., Saddoris, M. P., & Burwell, R. D. (2016). Subcortical connections of the perirhinal, postrhinal, and entorhinal cortices of the rat. II. efferents: SUBCORTICAL EFFERENTS OF PERIRHINAL, POSTRHINAL, & ENTORHINAL CORTICES. *Hippocampus*, *26*(9), 1213–1230. https://doi.org/10.1002/hipo.22600

Aminoff, E. M., Kveraga, K., & Bar, M. (2013). The role of the parahippocampal cortex in cognition. *Trends in Cognitive Sciences*, *17*(8), 379–390. https://doi.org/10.1016/j.tics.2013.06.009

Arnold, A. E. G. F., Ekstrom, A. D., & Iaria, G. (2018). Dynamic Neural Network Reconfiguration During the Generation and Reinstatement of Mnemonic Representations. *Frontiers in Human Neuroscience*, *12*, 292. https://doi.org/10.3389/fnhum.2018.00292

Baldwin, M. K. L., Balaram, P., & Kaas, J. H. (2017). The evolution and functions of nuclei of the visual pulvinar in primates: BALDWIN et al. *Journal of Comparative Neurology*, *525*(15), 3207–3226. https://doi.org/10.1002/cne.24272

Bar, M., & Aminoff, E. (2003). Cortical analysis of visual context. *Neuron*, *38*(2), 347–358. https://doi.org/10.1016/s0896-6273(03)00167-3

Bar, M., Aminoff, E., & Schacter, D. L. (2008). Scenes Unseen: The Parahippocampal Cortex Intrinsically Subserves Contextual Associations, Not Scenes or Places Per Se. *Journal of Neuroscience*, *28*(34), 8539–8544. https://doi.org/10.1523/JNEUROSCI.0987-08.2008

Beaudin, S. A., Singh, T., Agster, K. L., & Burwell, R. D. (2013). Borders and Comparative Cytoarchitecture of the Perirhinal and Postrhinal Cortices in an F1 Hybrid Mouse. *Cerebral Cortex*, *23*(2), 460–476. https://doi.org/10.1093/cercor/bhs038

Beer, Z., Chwiesko, C., Kitsukawa, T., & Sauvage, M. M. (2013). Spatial and stimulus-type tuning in the LEC, MEC, POR, PrC, CA1, and CA3 during spontaneous item recognition memory: Spatial and Stimulus-Type Tunings in Recognition Memory. *Hippocampus*, *23*(12), 1425–1438. https://doi.org/10.1002/hipo.22195

Beltramo, R. (2020). A new primary visual cortex. *Science*, *370*(6512), 46.2-46. https://doi.org/10.1126/science.abe1482

Beltramo, R., & Scanziani, M. (2019). A collicular visual cortex: Neocortical space for an ancient midbrain visual structure. *Science*, *363*(6422), 64–69. https://doi.org/10.1126/science.aau7052

Bragin, A., Jando, G., Nadasdy, Z., Hetke, J., Wise, K., & Buzsaki, G. (1995). Gamma (40-100 Hz) oscillation in the hippocampus of the behaving rat. *The Journal of Neuroscience*, *15*(1), 47–60. https://doi.org/10.1523/JNEUROSCI.15-01-00047.1995

Bucci, D. J. (2009). Posterior parietal cortex: An interface between attention and learning? *Neurobiology of Learning and Memory*, *91*(2), 114–120. https://doi.org/10.1016/j.nlm.2008.07.004

Bucci, D. J., & Burwell, R. D. (2004). Deficits in Attentional Orienting Following Damage to the Perirhinal or Postrhinal Cortices. *Behavioral Neuroscience*, *118*(5), 1117–1122. https://doi.org/10.1037/0735-7044.118.5.1117

Bucci, D. J., Phillips, R. G., & Burwell, R. D. (2000). Contributions of postrhinal and perirhinal cortex to contextual information processing. *Behavioral Neuroscience*, *114*(5), 882–894. https://doi.org/10.1037//0735-7044.114.5.882

Bucci, D. J., & Robinson, S. (2014). Toward a conceptualization of retrohippocampal contributions to learning and memory. *Neurobiology of Learning and Memory*, *116*, 197–207. https://doi.org/10.1016/j.nlm.2014.05.007

Bucci, D. J., Saddoris, M. P., & Burwell, R. D. (2002). Contextual fear discrimination is impaired by damage to the postrhinal or perirhinal cortex. *Behavioral Neuroscience*, *116*(3), 479–488.

Burgess, C. R., Ramesh, R. N., Sugden, A. U., Levandowski, K. M., Minnig, M. A., Fenselau, H., Lowell, B. B., & Andermann, M. L. (2016). Hunger-Dependent Enhancement of Food Cue Responses in

Mouse Postrhinal Cortex and Lateral Amygdala. *Neuron*, *91*(5), 1154–1169. https://doi.org/10.1016/j.neuron.2016.07.032

Burwell, R. D. (2001). Borders and cytoarchitecture of the perirhinal and postrhinal cortices in the rat: Perirhinal and Postrhinal Borders and Cytoarchitecture. *Journal of Comparative Neurology*, *437*(1), 17–41. https://doi.org/10.1002/cne.1267

Burwell, R. D. (2006). The Parahippocampal Region: Corticocortical Connectivity. *Annals of the New York Academy of Sciences*, *911*(1), 25–42. https://doi.org/10.1111/j.1749-6632.2000.tb06717.x

Burwell, R. D., & Agster, K. L. (2008). Anatomy of the Hippocampus and the Declarative Memory System. In *Learning and Memory: A Comprehensive Reference* (pp. 47–66). Elsevier. https://doi.org/10.1016/B978-012370509-9.00117-0

Burwell, R. D., & Amaral, D. G. (1998a). Perirhinal and postrhinal cortices of the rat: Interconnectivity and connections with the entorhinal cortex. *The Journal of Comparative Neurology*, *391*(3), 293–321. https://doi.org/10.1002/(sici)1096-9861(19980216)391:3<293::aid-cne2>3.0.co;2-x

Burwell, R. D., & Amaral, D. G. (1998b). Cortical afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. *The Journal of Comparative Neurology*, *398*(2), 179–205. https://doi.org/10.1002/(sici)1096-9861(19980824)398:2<179::aid-cne3>3.0.co;2-y

Burwell, R. D., Bucci, D. J., Sanborn, M. R., & Jutras, M. J. (2004). Perirhinal and postrhinal contributions to remote memory for context. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *24*(49), 11023–11028. https://doi.org/10.1523/JNEUROSCI.3781-04.2004

Burwell, R. D., & Hafeman, D. M. (2003). Positional firing properties of postrhinal cortex neurons. *Neuroscience*, *119*(2), 577–588. https://doi.org/10.1016/s0306-4522(03)00160-x

Burwell, R. D., Saddoris, M. P., Bucci, D. J., & Wiig, K. (2004a). Corticohippocampal Contributions to Spatial and Contextual Learning. *Journal of Neuroscience*, *24*(15), 3826–3836. https://doi.org/10.1523/JNEUROSCI.0410-04.2004

Burwell, R. D., Saddoris, M. P., Bucci, D. J., & Wiig, K. A. (2004b). Corticohippocampal contributions to spatial and contextual learning. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *24*(15), 3826–3836. https://doi.org/10.1523/JNEUROSCI.0410-04.2004

Burwell, R. D., Witter, M. P., & Amaral, D. G. (1995). Perirhinal and postrhinal cortices of the rat: A review of the neuroanatomical literature and comparison with findings from the monkey brain. *Hippocampus*, *5*(5), 390–408. https://doi.org/10.1002/hipo.450050503

Bussey, T. J., Duck, J., Muir, J. L., & Aggleton, J. P. (2000). Distinct patterns of behavioural impairments resulting from fornix transection or neurotoxic lesions of the perirhinal and postrhinal cortices in the rat. *Behavioural Brain Research*, *111*(1–2), 187–202. https://doi.org/10.1016/s0166-4328(00)00155-8

Bussey, T. J., Muir, J. L., & Aggleton, J. P. (1999). Functionally dissociating aspects of event memory: The effects of combined perirhinal and postrhinal cortex lesions on object and place memory in the rat. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *19*(1), 495–502.

Buzsaki, G. (2004). Neuronal Oscillations in Cortical Networks. *Science*, *304*(5679), 1926–1929. https://doi.org/10.1126/science.1099745

Buzsáki, G. (2005). Theta rhythm of navigation: Link between path integration and landmark navigation, episodic and semantic memory. *Hippocampus*, *15*(7), 827–840. https://doi.org/10.1002/hipo.20113

Chrobak, J. J., & Amaral, D. G. (2007). Entorhinal cortex of the monkey: VII. Intrinsic connections. *The Journal of Comparative Neurology*, *500*(4), 612–633. https://doi.org/10.1002/cne.21200

Colby, C. L., & Goldberg, M. E. (1999). SPACE AND ATTENTION IN PARIETAL CORTEX. *Annual Review of Neuroscience*, *22*(1), 319–349. https://doi.org/10.1146/annurev.neuro.22.1.319

Colgin, L. L., Denninger, T., Fyhn, M., Hafting, T., Bonnevie, T., Jensen, O., Moser, M.-B., & Moser, E. I. (2009). Frequency of gamma oscillations routes flow of information in the hippocampus. *Nature*, *462*(7271), 353–357. https://doi.org/10.1038/nature08573

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience*, *3*(3), 201–215. https://doi.org/10.1038/nrn755

Davies, M., Machin, P., Sanderson, D., Pearce, J., & Aggleton, J. (2007). Neurotoxic lesions of the rat perirhinal and postrhinal cortices and their impact on biconditional visual discrimination tasks. *Behavioural Brain Research*, *176*(2), 274–283. https://doi.org/10.1016/j.bbr.2006.10.005

Deacon, T. W., Eichenbaum, H., Rosenberg, P., & Eckmann, K. W. (1983). Afferent connections of the perirhinal cortex in the rat. *The Journal of Comparative Neurology*, *220*(2), 168–190. https://doi.org/10.1002/cne.902200205

Decurtis, M., & Pare, D. (2004). The rhinal cortices: A wall of inhibition between the neocortex and the hippocampus. *Progress in Neurobiology*, *74*(2), 101–110. https://doi.org/10.1016/j.pneurobio.2004.08.005

Delatour, B., & Witter, M. P. (2002). Projections from the parahippocampal region to the prefrontal cortex in the rat: Evidence of multiple pathways. *The European Journal of Neuroscience*, *15*(8), 1400–1407.

Dolorfo, C. L., & Amaral, D. G. (1998). Entorhinal cortex of the rat: Organization of intrinsic connections. *The Journal of Comparative Neurology*, *398*(1), 49–82. https://doi.org/10.1002/(sici)1096-9861(19980817)398:1<49::aid-cne4>3.0.co;2-9

Eacott, M. J., Gaffan, D., & Murray, E. A. (1994). Preserved recognition memory for small sets, and impaired stimulus identification for large sets, following rhinal cortex ablations in monkeys. *The European Journal of Neuroscience*, *6*(9), 1466–1478. https://doi.org/10.1111/j.1460-9568.1994.tb01008.x

Eacott, M. J., & Gaffan, E. A. (2005). The roles of perirhinal cortex, postrhinal cortex, and the fornix in memory for objects, contexts, and events in the rat. *The Quarterly Journal of Experimental Psychology. B, Comparative and Physiological Psychology*, *58*(3–4), 202–217. https://doi.org/10.1080/02724990444000203

Eichenbaum, H. (2000). A cortical-hippocampal system for declarative memory. *Nature Reviews. Neuroscience*, *1*(1), 41–50. https://doi.org/10.1038/35036213

Eichenbaum, H. (2017). The role of the hippocampus in navigation is memory. *Journal of Neurophysiology*, *117*(4), 1785–1796. https://doi.org/10.1152/jn.00005.2017

Eichenbaum, H., & Cohen, N. J. (2004). *From Conditioning to Conscious Recollection*. Oxford University Press. https://doi.org/10.1093/acprof:oso/9780195178043.001.0001

Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The Medial Temporal Lobe and Recognition Memory. *Annual Review of Neuroscience*, *30*(1), 123–152. https://doi.org/10.1146/annurev.neuro.30.051606.094328

Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends in Cognitive Sciences*, *12*(10), 388–396. https://doi.org/10.1016/j.tics.2008.07.004

Epstein, R. A., Parker, W. E., & Feiler, A. M. (2007). Where Am I Now? Distinct Roles for Parahippocampal and Retrosplenial Cortices in Place Recognition. *Journal of Neuroscience*, *27*(23), 6141–6149. https://doi.org/10.1523/JNEUROSCI.0799-07.2007

Estela-Pro, V. J. (2021). Neural correlates of early- and late-stage learning in the hippocampus and postrhinal cortex. *Neuroscience Theses and Dissertations*. Brown Digital Repository. Brown University Library.

Furtak, S. C., Ahmed, O. J., & Burwell, R. D. (2012). Single Neuron Activity and Theta Modulation in Postrhinal Cortex during Visual Object Discrimination. *Neuron*, *76*(5), 976–988. https://doi.org/10.1016/j.neuron.2012.10.039

Furtak, S. C., Wei, S.-M., Agster, K. L., & Burwell, R. D. (2007). Functional neuroanatomy of the parahippocampal region in the rat: The perirhinal and postrhinal cortices. *Hippocampus*, *17*(9), 709–722. https://doi.org/10.1002/hipo.20314

Gaffan, E. A., Healey, A. N., & Eacott, M. J. (2004). Objects and positions in visual scenes: Effects of perirhinal and postrhinal cortex lesions in the rat. *Behavioral Neuroscience*, *118*(5), 992–1010. https://doi.org/10.1037/0735-7044.118.5.992

Ghosh, M., Shanahan, B. E., Furtak, S. C., Mashour, G. A., Burwell, R. D., & Ahmed, O. J. (2020). *Instantaneous amplitude and shape of postrhinal theta oscillations differentially encode running speed* [Preprint]. Neuroscience. https://doi.org/10.1101/2020.06.03.130609

Glasgow, S. D., & Chapman, C. A. (2007). Local Generation of Theta-Frequency EEG Activity in the Parasubiculum. *Journal of Neurophysiology*, *97*(6), 3868–3879. https://doi.org/10.1152/jn.01306.2006

Gosselin, N. (2006). Emotional responses to unpleasant music correlates with damage to the parahippocampal cortex. *Brain*, *129*(10), 2585–2592. https://doi.org/10.1093/brain/awl240

Hafting, T., Fyhn, M., Molden, S., Moser, M.-B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature*, *436*(7052), 801–806. https://doi.org/10.1038/nature03721

Howard, L. R., Kumaran, D., Olafsdottir, H. F., & Spiers, H. J. (2011). Double Dissociation between Hippocampal and Parahippocampal Responses to Object-Background Context and Scene Novelty. *Journal of Neuroscience*, *31*(14), 5253–5261. https://doi.org/10.1523/JNEUROSCI.6055-10.2011

Hwang, E., Willis, B. S., & Burwell, R. D. (2018). Prefrontal connections of the perirhinal and postrhinal cortices in the rat. *Behavioural Brain Research*, *354*, 8–21. https://doi.org/10.1016/j.bbr.2017.07.032

Jones, M. W., & Wilson, M. A. (2005). Theta Rhythms Coordinate Hippocampal–Prefrontal Interactions in a Spatial Memory Task. *PLoS Biology*, *3*(12), e402. https://doi.org/10.1371/journal.pbio.0030402

Kaas, J. H., & Baldwin, M. K. L. (2019). The Evolution of the Pulvinar Complex in Primates and Its Role in the Dorsal and Ventral Streams of Cortical Processing. *Vision*, *4*(1), 3. https://doi.org/10.3390/vision4010003

Kepecs, A., Uchida, N., & Mainen, Z. F. (2006). The Sniff as a Unit of Olfactory Processing. *Chemical Senses*, *31*(2), 167–179. https://doi.org/10.1093/chemse/bjj016

Kinnavane, L., Amin, E., Olarte-Sánchez, C. M., & Aggleton, J. P. (2017). Medial temporal pathways for contextual learning: Network c- *fos* mapping in rats with or without perirhinal cortex lesions. *Brain and Neuroscience Advances*, *1*, 239821281769416. https://doi.org/10.1177/2398212817694167

Knierim, J. J., Lee, I., & Hargreaves, E. L. (2006). Hippocampal place cells: Parallel input streams, subregional processing, and implications for episodic memory. *Hippocampus*, *16*(9), 755–764. https://doi.org/10.1002/hipo.20203

Koganezawa, N., Gisetstad, R., Husby, E., Doan, T. P., & Witter, M. P. (2015). Excitatory Postrhinal Projections to Principal Cells in the Medial Entorhinal Cortex. *Journal of Neuroscience*, *35*(48), 15860–15874. https://doi.org/10.1523/JNEUROSCI.0653-15.2015

Komorowski, R. W., Manns, J. R., & Eichenbaum, H. (2009). Robust Conjunctive Item-Place Coding by Hippocampal Neurons Parallels Learning What Happens Where. *Journal of Neuroscience*, *29*(31), 9918–9929. https://doi.org/10.1523/JNEUROSCI.1378-09.2009

Kroemer, N. B., Burrasch, C., & Hellrung, L. (2016). To work or not to work. In *Progress in Brain Research* (Vol. 229, pp. 125–157). Elsevier. https://doi.org/10.1016/bs.pbr.2016.06.009

Kropff, E., Carmichael, J. E., Moser, M.-B., & Moser, E. I. (2015). Speed cells in the medial entorhinal cortex. *Nature*, *523*(7561), 419–424. https://doi.org/10.1038/nature14622

Kuang, S., Morel, P., & Gail, A. (2015). Planning Movements in Visual and Physical Space in Monkey Posterior Parietal Cortex. *Cerebral Cortex*, bhu312. https://doi.org/10.1093/cercor/bhu312

LaChance, P. A., Todd, T. P., & Taube, J. S. (2019). A sense of space in postrhinal cortex. *Science*, *365*(6449), eaax4192. https://doi.org/10.1126/science.aax4192

Liu, P., & Bilkey, D. K. (2002). The effects of NMDA lesions centered on the postrhinal cortex on spatial memory tasks in the rat. *Behavioral Neuroscience*, *116*(5), 860–873. https://doi.org/10.1037/0735-7044.116.5.860

Mathur, B. N. (2014). The claustrum in review. *Frontiers in Systems Neuroscience*, *8*. https://doi.org/10.3389/fnsys.2014.00048

Meier, A. M., Wang, Q., Ji, W., Ganachaud, J., & Burkhalter, A. (2021). Modular Network between Postrhinal Visual Cortex, Amygdala, and Entorhinal Cortex. *The Journal of Neuroscience*, *41*(22), 4809–4825. https://doi.org/10.1523/JNEUROSCI.2185-20.2021

Mitchell, S. J., & Ranck, J. B. (1980). Generation of theta rhythm in medial entorhinal cortex of freely moving rats. *Brain Research*, *189*(1), 49–66. https://doi.org/10.1016/0006-8993(80)90006-2

Naber, P. A., Caballero-Bleda, M., Jorritsma-Byham, B., & Witter, M. P. (1997). Parallel input to the hippocampal memory system through peri- and postrhinal cortices. *Neuroreport*, *8*(11), 2617–2621. https://doi.org/10.1097/00001756-199707280-00039

Naber, P. A., Witter, M. P., & Lopes da Silva, F. H. (2001). Evidence for a direct projection from the postrhinal cortex to the subiculum in the rat. *Hippocampus*, *11*(2), 105–117. https://doi.org/10.1002/hipo.1029

Nerad, L., & McNaughton, N. (2006). The septal EEG suggests a distributed organization of the pacemaker of hippocampal theta in the rat. *European Journal of Neuroscience*, *24*(1), 155–166. https://doi.org/10.1111/j.1460-9568.2006.04902.x

Nishio, N., Tsukano, H., Hishida, R., Abe, M., Nakai, J., Kawamura, M., Aiba, A., Sakimura, K., & Shibuki, K. (2018). Higher visual responses in the temporal cortex of mice. *Scientific Reports*, *8*(1), 11136. https://doi.org/10.1038/s41598-018-29530-3

Norman, G., & Eacott, M. J. (2005). Dissociable effects of lesions to the perirhinal cortex and the postrhinal cortex on memory for context and objects in rats. *Behavioral Neuroscience*, *119*(2), 557–566. https://doi.org/10.1037/0735-7044.119.2.557

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, *34*(1), 171–175. https://doi.org/10.1016/0006-8993(71)90358-1

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Clarendon Press ; Oxford University Press.

Passetti, F., Chudasama, Y., & Robbins, T. W. (2002). The frontal cortex of the rat and visual attentional performance: Dissociable functions of distinct medial prefrontal subregions. *Cerebral Cortex (New York, N.Y.: 1991)*, *12*(12), 1254–1268. https://doi.org/10.1093/cercor/12.12.1254

Peck, J. R., & Taube, J. S. (2017). The postrhinal cortex is not necessary for landmark control in rat head direction cells: Postrhinal Cortex Lesions and Landmark Control. *Hippocampus*, *27*(2), 156–168. https://doi.org/10.1002/hipo.22680

Peng, X., & Burwell, R. D. (2021). Beyond the hippocampus: The role of parahippocampal-prefrontal communication in context-modulated behavior. Neurobiology of Learning and Memory, 107520. https://doi.org/10.1016/j.nlm.2021.107520

Posner, M. I., & Petersen, S. E. (1990). The Attention System of the Human Brain. *Annual Review of Neuroscience*, *13*(1), 25–42. https://doi.org/10.1146/annurev.ne.13.030190.000325

Posner, M. I., Rothbart, M. K., & The American Association for Research into Nervous and Mental Diseases. (1998). Attention, self–regulation and consciousness. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *353*(1377), 1915–1927. https://doi.org/10.1098/rstb.1998.0344

Posner, M. I., Walker, J. A., Friedrich, F. J., & Rafal, R. D. (1984). Effects of parietal injury on covert orienting of attention. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *4*(7), 1863–1874.

Qi, X., Du, Z. J., Zhu, L., Liu, X., Xu, H., Zhou, Z., Zhong, C., Li, S., Wang, L., & Zhang, Z. (2019). The Glutamatergic Postrhinal Cortex–Ventrolateral Orbitofrontal Cortex Pathway Regulates Spatial Memory Retrieval. *Neuroscience Bulletin*, *35*(3), 447–460. https://doi.org/10.1007/s12264-018-0325-4

Ramos, J. M. J. (2013). Differential contribution of hippocampus, perirhinal cortex and postrhinal cortex to allocentric spatial memory in the radial maze. *Behavioural Brain Research*, *247*, 59–64. https://doi.org/10.1016/j.bbr.2013.03.017

Reep, R. L., & Corwin, J. V. (2009). Posterior parietal cortex as part of a neural network for directed attention in rats. *Neurobiology of Learning and Memory*, *91*(2), 104–113. https://doi.org/10.1016/j.nlm.2008.08.010

Scaplen, K. M., Agster, K. L., & Burwell, R. D. (2017). Anatomy of the Hippocampus and the Declarative Memory System. In *J. H. Byrne (Ed.), Concise Learning and Memory* (1st ed.). Academic Press.

Scaplen, K. M., Gulati, A. A., Heimer-McGinn, V. L., & Burwell, R. D. (2014). Objects and landmarks: Hippocampal place cells respond differently to manipulations of visual cues depending on size, perspective, and experience: Hippocampal Place Cell Responses To Landmarks and Objects. *Hippocampus*, *24*(11), 1287–1299. https://doi.org/10.1002/hipo.22331

Scaplen, K. M., Ramesh, R. N., Nadvar, N., Ahmed, O. J., & Burwell, R. D. (2017). Inactivation of the Lateral Entorhinal Area Increases the Influence of Visual Cues on Hippocampal Place Cell Activity. *Frontiers in Systems Neuroscience*, *11*, 40. https://doi.org/10.3389/fnsys.2017.00040

Seidenbecher, T. (2003). Amygdalar and Hippocampal Theta Rhythm Synchronization During Fear Memory Retrieval. *Science*, *301*(5634), 846–850. https://doi.org/10.1126/science.1085818

Sills, J. B., Connors, B. W., & Burwell, R. D. (2012). Electrophysiological and morphological properties of neurons in layer 5 of the rat postrhinal cortex. *Hippocampus*, *22*(9), 1912–1922. https://doi.org/10.1002/hipo.22026

Smith, A. P. R., Henson, R. N. A., Dolan, R. J., & Rugg, M. D. (2004). FMRI correlates of the episodic retrieval of emotional contexts. *NeuroImage*, *22*(2), 868–878. https://doi.org/10.1016/j.neuroimage.2004.01.049

Smith, D. M., & Mizumori, S. J. Y. (2006). Hippocampal place cells, context, and episodic memory. *Hippocampus*, *16*(9), 716–729. https://doi.org/10.1002/hipo.20208

Squire, L. R., Stark, C. E. L., & Clark, R. E. (2004). The medial temporal lobe. *Annual Review of Neuroscience*, *27*, 279–306. https://doi.org/10.1146/annurev.neuro.27.070203.144130

Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences*, *93*(24), 13515–13522. https://doi.org/10.1073/pnas.93.24.13515

Sugden, A. U. (2015). Diverse subtypes of fast-spiking inhibitory neurons in neocortex. *Molecular Biology, Cell Biology, and Biochemistry Theses and Dissertations.* Brown Digital Repository. Brown University Library. https://doi.org/10.7301/Z0QC01WF

Suzuki, W. A. (2007). Making New Memories: The Role of the Hippocampus in New Associative Learning. *Annals of the New York Academy of Sciences*, *1097*(1), 1–11. https://doi.org/10.1196/annals.1379.007

Tomás Pereira, I., Agster, K. L., & Burwell, R. D. (2016). Subcortical connections of the perirhinal, postrhinal, and entorhinal cortices of the rat. I. afferents: SUBCORTICAL AFFERENTS OF PERIRHINAL, POSTRHINAL, AND ENTORHINAL CORTICES. *Hippocampus*, *26*(9), 1189–1212. https://doi.org/10.1002/hipo.22603

Tsao, A., Sugar, J., Lu, L., Wang, C., Knierim, J. J., Moser, M.-B., & Moser, E. I. (2018). Integrating time from experience in the lateral entorhinal cortex. *Nature*, *561*(7721), 57–62. https://doi.org/10.1038/s41586-018-0459-6

Tulving, E., & Markowitsch, H. J. (1998). Episodic and declarative memory: Role of the hippocampus. *Hippocampus*, *8*(3), 198–204. https://doi.org/10.1002/(SICI)1098-1063(1998)8:3<198::AID-HIPO2>3.0.CO;2-G

Uylings, H. B. M., Groenewegen, H. J., & Kolb, B. (2003). Do rats have a prefrontal cortex? *Behavioural Brain Research*, *146*(1–2), 3–17. https://doi.org/10.1016/j.bbr.2003.09.028

van Kesteren, M. T. R., Brown, T. I., & Wagner, A. D. (2018). Learned Spatial Schemas and Prospective Hippocampal Activity Support Navigation After One-Shot Learning. *Frontiers in Human Neuroscience*, *12*, 486. https://doi.org/10.3389/fnhum.2018.00486

Vogt, B. A., & Miller, M. W. (1983). Cortical connections between rat cingulate cortex and visual, motor, and postsubicular cortices. *The Journal of Comparative Neurology*, *216*(2), 192–210. https://doi.org/10.1002/cne.902160207

Wang, C., Chen, X., Lee, H., Deshmukh, S. S., Yoganarasimha, D., Savelli, F., & Knierim, J. J. (2018). Egocentric coding of external items in the lateral entorhinal cortex. *Science*, *362*(6417), 945–949. https://doi.org/10.1126/science.aau4940

Wirth, S., Yanike, M., Frank, L. M., Smith, A. C., Brown, E. N., & Suzuki, W. A. (2003). Single neurons in the monkey hippocampus and learning of new associations. *Science (New York, N.Y.)*, *300*(5625), 1578–1581. https://doi.org/10.1126/science.1084324

Witter, M. P. (2010). Connectivity of the Hippocampus. In V. Cutsuridis, B. Graham, S. Cobb, & I. Vida (Eds.), *Hippocampal Microcircuits* (pp. 5–26). Springer New York. https://doi.org/10.1007/978-1-4419-0996-1_1

Yang, F.-C., & Burwell, R. D. (2020). Neuronal Activity in the Rat Pulvinar Correlates with Multiple Higher-Order Cognitive Functions. *Vision*, *4*(1), 15. https://doi.org/10.3390/vision4010015

Figures and Figure Legends

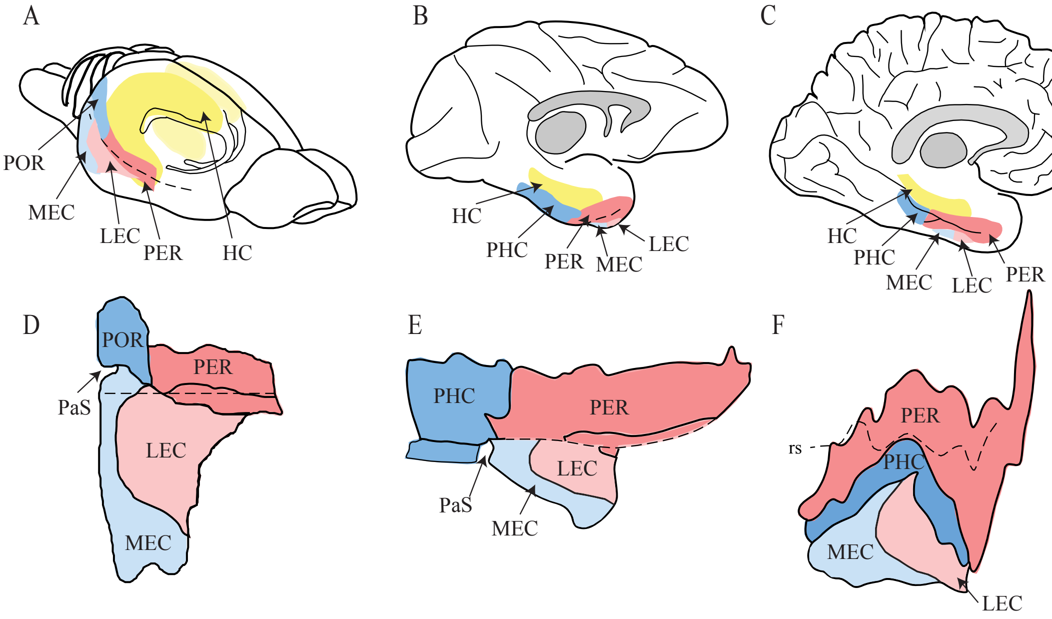

Figure 1. Surface views and unfolded maps for the parahippocampal region. A. Oblique surface view of the rat brain showing perirhinal (PER) areas 35 and 36, the postrhinal cortex (POR), the lateral entorhi-nal cortex (LEC), the medial entorhinal cortex (MEC), and the hippocampus (HC). (B) Mid-sagittal schematic of the monkey brain showing the PER, HC, the parahippocampal cortex (PHC), the primate homolog of the rodent POR, and the LEC and MEC. C. Mid-sagittal schematic of the human brain show-ing the PER, PHC, EC, and HC using the same color scheme. D-F. Shown are unfolded maps of the PER, POR/PHC, and EC for the rodent (D), monkey (E), and human (F) brains. Other abbreviations: PaS, parasubiculum; rs, rhinal sulcus.

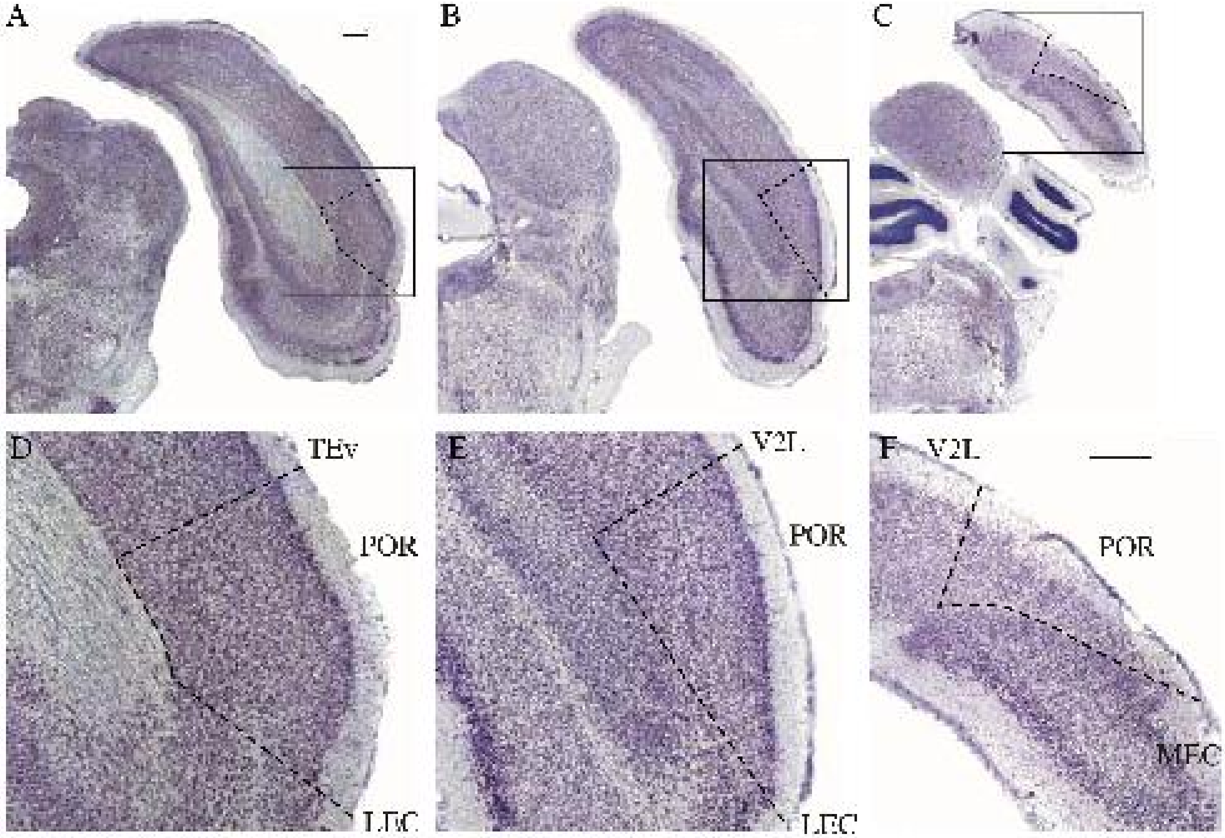

Figure 2. Nissle-stained coronal sections showing the POR and adjacent cortical regions at three rostrocaudal levels: -7.68 mm, -8.40, and -9.12 relative to Bregma. Scale bar = 500 um. Boxes in A-C correspond to panels D-F, respectively. Other abbreviations: TEv, ventral temporal cortex; LEC, lateral entorhinal cortex; MEC, medial entorhinal cortex; V2L, second-ary visual cortex lateral area.

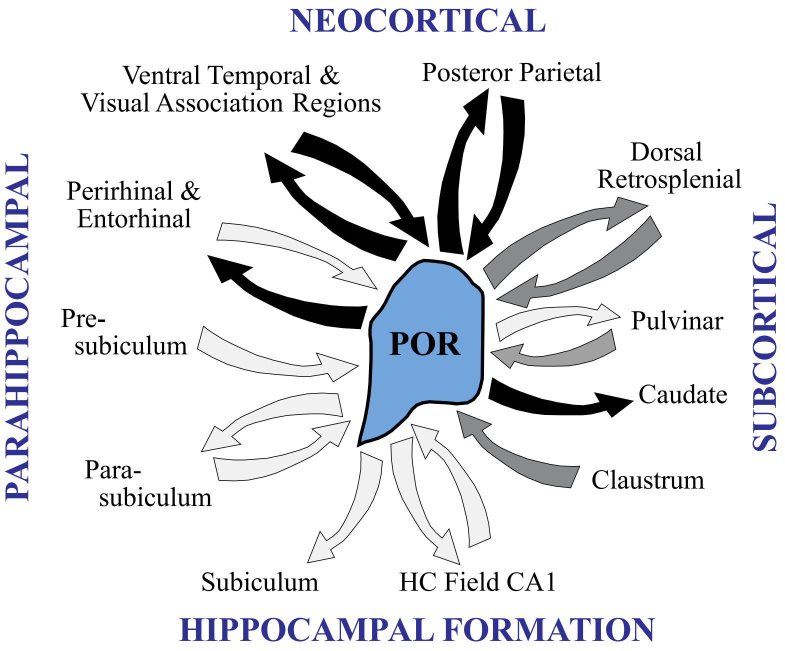

Figure 3. Schematic summarizing the cortical, subcortical, hippocampal (HC), and parahippocampal afferent and efferent connections of the postrhinal cortex (POR). Toward the top are the cortical efferents and afferents. On the left are the connections with the structures in the parahippocampal regions. On the right are the strongest connections with subcortical regions. On the bottom are connections with hippocam-pal formation structures. Note, strong connections are represented by black arrows, moderate connections are denoted by dark gray arrows, and weak connections are indicated by the light gray arrows.

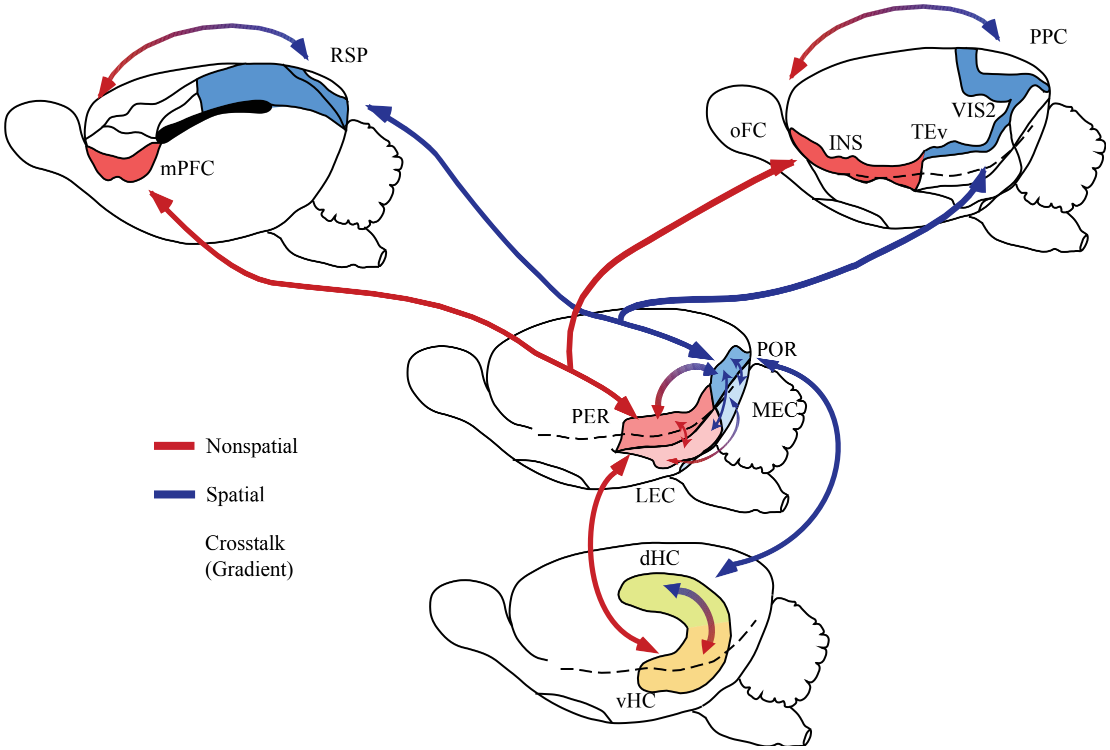

Figure 4. Schematic of dorsal and ventral visual stream inputs to the medial temporal lobe memory system. Arrows show the flow of spatial and non-spatial information, as well as connections across the two information processing streams. Much of the spatial information arises from the retrosplenial (RSP) and posterior parietal (PPC) cortices and it preferentially targets the postrhinal cortex (POR), whereas non-spatial information tends to arise from frontal areas and preferentially targets the perirhinal cortex (PER). What is under-appreciated in the field is the extent to which there is cross-talk at every level of the hierarchy (see dual color arrows). Other abbreviations: dHC, dorsal hippocampus; INS, insula; LEC, lateral entorhinal cortex; MEC, medial entorhinal cortex; mPFC, medial prefrontal cortex; oFC, orbital frontal cortex; TEv, ventral temporal cortex; vHC, ventral hippocampus; VIS2, secondary visual cortex.

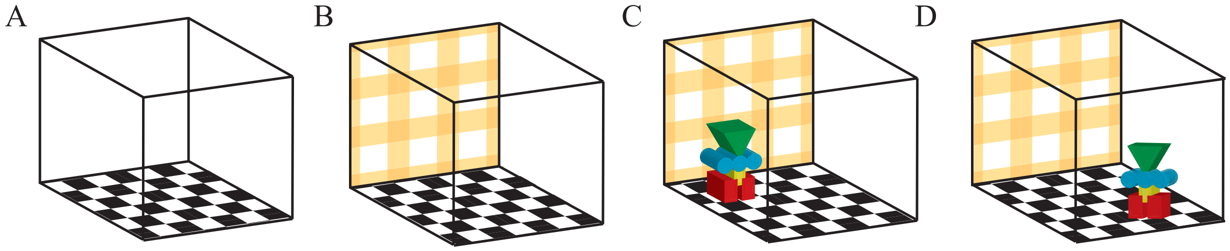

Figure 5. Illustrated model of POR involvement in the processing of information about the geometry of a space and other features such as the pattern on a floor. B. POR may signal changes in the environment such as an altered pattern on the wall. C. POR also appears to encode the spatial layout of objects in the local context. D. POR may also signal when there are changes in the spatial layout of objects, e.g., the transition from c to d.

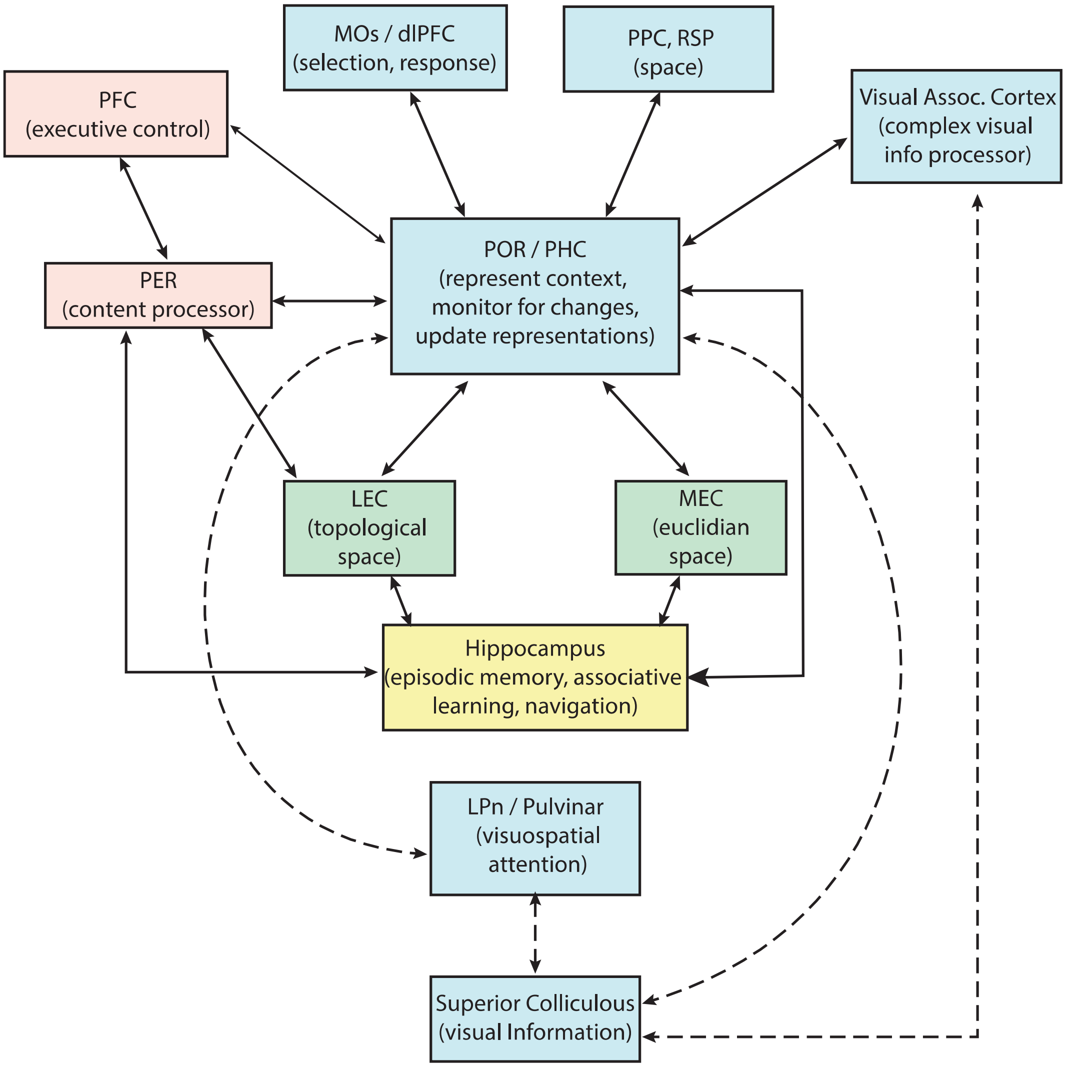

Figure 6. Updated model to represent the documented roles and connections of the postrhinal cortex in the medial temporal network. Visual information from primary visual areas, superior colliculus, and visual association cortex, spatial information from the retrosplenial (RSP), and posterior parietal (PPC) cortices as well as attentional information from secondary motor cortex (MOs) and the thalamic pulvinar (also called the lateral posterior nucleus (LPn) in the rodent) preferentially target the rodent posthinal cortex (POR), homolog of the primate parahippocampal cortex (PHC). MOs may be the rodent homolog of the primate dorsolateral prefrontal cortex (dlPFC). Processed context information from the POR is then used by many regions such as prefrontal cortex (PFC) regarding context-guided decision making and the hippocampus for context-guided associative learning and episodic memory. Other abbreviations: LEC, lateral entorhinal cortex; MEC, medial entorhinal cortex.