

Post-print:**How the Brain's Navigation System Shapes Our Visual Experience.**

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o.1 Abstract

We explore the environment not only by navigating, but also by viewing our surroundings with our eyes. Here we review growing evidence that the mammalian hippocampal formation, extensively studied in the context of navigation and memory, mediates a representation of visual space that is stably anchored to the external world. This visual representation puts the hippocampal formation in a central position to guide viewing behavior and to modulate visual processing beyond the medial temporal lobe (MTL). We suggest that vision and navigation share several key computational challenges that are solved by overlapping and potentially common neural systems, making vision an optimal domain to explore whether and how the MTL supports cognitive operations beyond navigation.

O.2 All eyes on the hippocampal formation

Navigation and vision are two fundamental strategies used to explore the world, and how we use one often directly affects how we use the other [1,2]. Like navigation—defined here as physical body-based movement through the environment—, eye movements make it possible to acquire new information rapidly. However, they also introduce a critical problem that the brain must solve: each time the eyes move, all features in the visual scene change their position relative to the retina (self-centered reference, see Glossary), and yet our subjective experience is that their location remains stably defined in external world-based coordinates (world-centered reference). Such world-centered coordinates are useful; they not only stabilize perception, but also are critical to efficiently accomplish many actions, such as visual search or reaching. Despite decades of research revealing several interconnected mechanisms, how the brain generates and maintains world-centered representations of visual space remains unclear. Here we suggest a possible solution to this problem, based on how the brain solves a parallel problem in the navigational domain.

There are two primary ways navigators keep track of their position as they move. First, navigators can use path integration to keep track of their displacement, a process that involves the use of internal self-motion cues (e.g., vestibular or proprioceptive signals) without reference to the external world [3,4]. A limitation of this strategy, however, is that tracking errors inevitably accumulate over time. Thus, an alternate strategy is world-centered navigation, which involves the use of external sensory cues to maintain a representation of navigable space that is invariant to one's own movements [5]. A key mediator of world-centered coding during navigation is the hippocampal formation (HF) [6,7]. Here we review growing evidence that the HF not only supports world-centered navigation, but also represents world-centered visual space as well. This observation implies that this article's very own title is somewhat misleading. Referring to the HF as 'the brain's navigation system' does not capture the full range of cognitive functions it supports. Visual exploration and navigation might in fact not be two parallel operations, but may rather be two expressions of a common mechanism for exploring the world.

0.3 Medial temporal codes support navigation and vision

The hippocampus contains place cells that fire whenever a navigator occupies particular environmental locations [8]. Different place cells fire in different locations and thus, as a population, represent a world-centered map of navigable space. Place cells use self-motion information to maintain spatial representations in darkness for a short time, but eventually accumulate errors over longer timescales that are corrected using external sensory cues [9,10]. Intriguingly, place cells also have an entirely visual analogue. Specifically, the primate hippocampus contains neurons that increase firing rate when specific environmental locations are viewed, irrespective of the location of the body, eye position in the orbit, or facing direction (Figure 1A, Key Figure) [11,12]. These spatial view cells are updated based on eye movements when the preferred view is hidden in darkness or obscured, but tend to drift and become less sharply tuned [13]. Therefore, spatial view cells have similar properties as place cells, except tuned to world-centered gaze location instead of self-location. Place cells are not topographically organized in the rodent hippocampus [14] (i.e., cells tuned to nearby environmental locations are not more anatomically proximal than cells tuned to far apart locations), which may explain why previous studies did not observe a topographically organized representation of visual space in the hippocampus [15]. Notably, the presence of a world-centered map of visual space in the hippocampus does not necessarily imply that the hippocampus is involved in visual perception per se beyond providing a coordinate system (see Box 1 for further discussion).

One of the primary inputs to the hippocampus is the entorhinal cortex (EC). During navigation, entorhinal grid cells fire in a regular hexagonal lattice of locations that tile the floor of the environment [16]. Grid cells are thought to combine self-motion and environmental information to provide a stable metric for the place cell map [17]. Similar to grid cells, recordings of EC neurons in head-fixed monkeys revealed strikingly similar hexagonal firing patterns encoding the location of gaze during free viewing of visual scenes (Figure 1B) [18]. A proportion of these visual grid cells shift their firing fields in concert with translation of the visual scene, showing that some represent visual space in world-centered coordinates (Figure 1C) [19]. In two recent studies, we extended these findings by showing that also human EC supports a world-centered grid-like representation of visual space [20, 21].

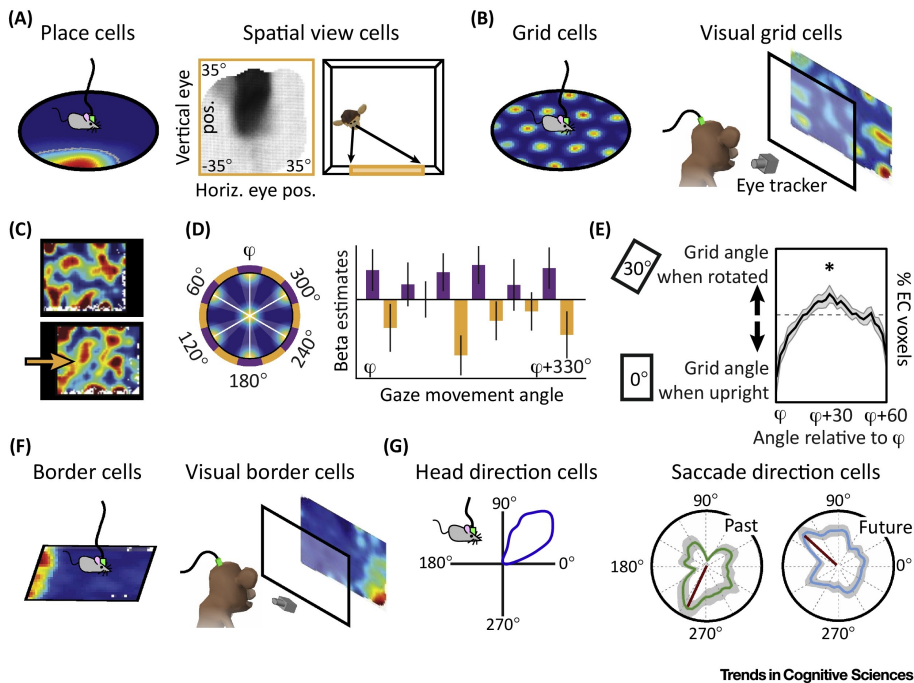


Figure 1: Key Figure: Spatial Codes in Vision and Navigation. (A) Place cells and spatial view cells in hippocampus. Left: rodent place cells encode self-location in the world (firing rate color-coded). Right: monkey spatial view cells encode world-centered gaze location (firing rate in dark color); example cell from [12]. (B) Grid cells and visual grid cells in entorhinal cortex (EC). Left: grid cells fire at several locations arranged in hexagonal lattice tiling the environment. Right: monkey visual grid cells show the same hexagonal firing but encode gaze position in the visual scene (adapted from [18]). (C) Grid pattern anchors to boundary. Firing pattern of some visual grid cells shifts (yellow arrow) in concert with shifts in the stimulus (adapted from [19]). (D) Human fMRI-grid signature. Left: visual grid cell model predicts higher activity for gaze directions parallel to the grid axes (φ and steps of 60° , white lines) than for directions in between. Right: fMRI activity in EC depends on gaze direction showing predicted sixfold rotational symmetry. (E) Visual boundary anchoring of human fMRI-grid signature. When search display rotates during visual search, fMRI grid signature in most voxels changes orientation, mirroring the search display rotation. (F) Border cells and visual border cells in EC. Left: rodent border cells encode proximity to navigational boundaries. Right: visual border cells encode proximity of the monkey's gaze to the edges of a visual stimulus (example cell from [18]). (G) Head direction cells and saccade direction cells in EC. Left: rodent head direction cells encode facing direction. Right: monkey saccade direction cells encode direction of future and past saccades (adapted from [22]).

Participants had their gaze position monitored while they performed an object tracking or visual search task. fMRI responses in EC exhibited a sixfold symmetry as a function of gaze movement direction, which is indicative of grid cell activity (Figure 1D) and akin to the fMRI grid-signature found during navigation [23]. This

visual grid representation was absent when participants fixated but the visual scene was moved instead, suggesting that active movements of gaze or attention are required to drive visual grid cells. Passive transport likewise abolishes grid coding of navigable space in mice [24]. Critically, we also found that the EC visual grid signal is anchored to the visual scene in the same way as rodent grid cells representing navigable spaces [25,26], adopting reliable alignments to the borders of the visual stimulus and rotating in concert with rotation of these borders (Figure 1E).

Place and grid cell firing fields are likely anchored to the external world [27,28] by border cells in the EC and the subiculum that fire when navigators are a particular distance and direction from spatial boundaries [29–31]. Border cells are tuned not only to navigational obstacles like walls, but also to vertical cliffs, raising the possibility that such cells represent the edges of the local environment broadly [30]. Akin to border cells, monkey EC contains neurons that increase their firing rates when gaze is close to one or more of the borders of a visual stimulus [18] (Figure 1F). Visual border cells respond to the outer edges of a visual stimulus irrespective of the stimulus content. The borders of visual space have long been known to influence search efficiency in visual search tasks [32]. Importantly, unlike neurons in primary visual cortex tuned to orientated edges in retinotopic coordinates, visual border cells do not respond to edges within the visual stimulus itself.

Another critical component of the world-centered navigation system are head direction (HD) cells found in several subcortical and cortical structures, including EC [33]. HD cells fire based on the orientation of the head in the navigational plane, independent of body location, and are updated by a combination of vestibular and external sensory inputs, including visual information that references the HD signal to the environment [34]. Different HD cells have different preferred orientations and thus, as a population, are akin to a neural compass [33], likely acting in concert with border cells to orient place and grid cell firing fields relative to the external world. Similar to HD cells, neurons selective for eye movement direction were recently observed in monkey EC [22]. These saccade direction (SD) cells are tuned to the direction of an upcoming saccade or a previously completed saccade, or both, independent of the position the monkey is currently looking at in visual space (Figure 1G). Whether SD cells code direction in world-centered coordinates is unknown, but one possibility is that they represent SD relative to an axis defined by gravity.

Box 1. Is the hippocampal formation involved in visual perception?

Perceptual impairments following MTL damage, and MTL activation to visual stimuli, have raised the question whether the HF is involved in visual perception, independent of memory [35–37]. Some of the strongest evidence for this idea comes from studies examining hippocampal involvement in perception of visual scenes. In fMRI studies, hippocampal responses are stronger for visual scenes than for objects, even if no explicit task was performed [38], and several studies found that the ability to differentiate visual scenes depends on healthy hippocampal function [39–42]. Such results have led to the proposal that the hippocampus is an integral part of the visual scene perception network [43].

An alternate possibility is that hippocampal responses to visual stimuli reflect the extent to which perception requires coding of relational information. Visual scenes are defined not only by their local features, but also by the specific global arrangement of those features. Such global feature arrangements engage the HF more strongly than details in a visual scene [44], and increasing overlap between images interferes with recognition to a greater extent in individuals with MTL damage compared with healthy controls [39,42]. While the implications of such findings are still debated (e.g., [35,45]), they suggest that the role of the HF in visual perception may be the processing of relational information, rather than perception of visual content per se, a process not restricted solely to perception or memory. This also resonates well with reports that hippocampal patients are impaired at imagining scenes with high spatial coherence [46].

Such results may explain why MTL perceptual effects are most pronounced for visual scenes defined not only by specific features (e.g., vase and table), but also by the spatial arrangement of those scene features (e.g., the vase stands on the table versus the vase stands under the table). Relational coding requires a coordinate system relative to which the locations of visual features can be specified. The MTL might provide just such a world-centered coordinate system that is invariant to the specific content of the scene. This implicates the HF in visual perception insofar as relational processing is required. In addition, as we discuss in the Recall and Planning section, the MTL likely also plays a role in perception by guiding overt [18] and covert [47] perceptual sampling, possibly by forming predictions [48] that also modulate visual processing [49].

In support of this idea, the orientation of the head relative to the gravity axis affects perception of the orientation of visual stimuli [50,51]. The monkey anterior thalamus contains neurons that carry a gravity-anchored head orientation signal that could provide input to SD cells [52], similar to how thalamic HD cells serve as input to parahippocampal HD neurons in rodents [33]. These functional and

structural similarities suggest that primate SD cells may have an evolutionary origin similar to the rodent HD circuit [22].

In sum, each of the key neural mechanisms that represent a world-centered map (place cells, grid cells, border cells) and compass (HD cells) for navigation have purely visual analogues that encode a world-centered map of visual space (spatial view cells, visual grid cells, visual border cells) and the direction of eye movements (SD cells). The HF thus represents world-centered visual space using similar mechanisms as it does to encode world-centered navigable space, putting it at a key position to support computations in both domains. We suggest that the HF may provide the optimal solution to three key computational challenges shared by navigation and vision: reference frame transformations, recall and planning, and context specificity (which we will discuss below).

0.4 Reference frame transformations

All sensory information is self-centered, and yet our perceptual experience of the world is stable during movements. This remarkable phenomenon requires the brain to reconstruct self-motion invariant coordinates from noisy self-centered inputs [53], a computation critical for both navigation and vision. How we experience the world as stable despite variability in retinal input across eye movements (i.e., how the brain performs this transformation between reference frames) continues to be a matter of debate [54–56]. Consideration of the neural basis of such reference frame transformations during navigation suggests a possible solution by which self-centered visual representations are transformed into world-centered ones as well.

During navigation, self-centered coordinates are transformed into world-centered ones by a brain network consisting of the posterior parietal cortex (PPC), the medial parietal retrosplenial complex (RSC) that includes the retrosplenial and posterior cingulate cortices, and the HF [57–59] (Box 2). Each stage of this network contributes differentially to the two reference frames, with PPC mainly processing self-centered (often body-based) information, the HF encoding world-centered information, and RSC serving as the key transformation stage between the two [57, 58, 60]. This model suggests that the HF receives self-centered input from neocortex, and in turn projects world-centered coordinates back to guide navigational behavior [57, 59]. Coordinates are likely converted between the two reference frames by integrating external sensory information with proprioceptive

and vestibular signals related to self-motion and path integration [61].

Retinotopic representations of the visual field [62] are also likely transformed to world-centered ones by the PPC-RSC-MTL pathway. In PPC, some visual receptive fields are invariant to eye movements [63] (Figure 2A) and retinotopic representations are updated to compensate for eye displacement before eye movements are executed [64] (Figure 2B). This coordinate transformation is driven by integration of visual inputs with corollary discharges about impending eye movements [56], a process known as retinotopic updating [55, 65]. Retinotopic updating is also observed in a number of other brain regions [55] and similar mechanisms support non-retinotopic encoding of visual motion in several monkey [66] and human [67, 68] brain areas as well. It is often unclear which extra-retinal coordinate system these regions use to represent visual space, but head- and body-based coordinates have been observed. Moreover, some PPC neurons dynamically switch between reference frames depending on whether the direction of gaze is fixed relative to the head or body [69]. By integrating retinal information with self-motion signals, these regions compensate for self-induced changes to the visual scene and anticipate the consequences of future saccades [64, 65, 70]. However, retinotopic updating alone cannot account for a range of findings related to visual memory, such as head-centered (possibly world-centered) memory traces in retinotopic receptive fields [71] (Figure 2C). Moreover, like path integration, retinotopic updating is prone to error accumulation over time [72], as it requires constant updating of locations in the visual field, and thus a further corrective and stabilizing mechanism is needed.

One possibility is that visual representations in PPC, transformed to non-retinotopic coordinates by retinotopic updating and self-motion integration [56, 64, 73], serve as input to the HF, which then forms a robust world-centered map of visual space through predictive statistical learning [48]. The PPC-RSC pathway is well positioned for this signal transmission to the MTL [74] (Box 2). During navigation, RSC neurons in rodents encode turn direction, path position, and direction-dependent locations in route-based coordinates, as well as body orientation and location in multiple world-centered reference frames [75–78] (Figure 2D), in line with human imaging results [79, 80]. Analogously, the posterior portion of RSC represents visual space in retinotopic coordinates [81], and the posterior cingulate represents visual space in world-centered coordinates [82] (Figure 2E). Rodent RSC also signals head movement information directly to early visual regions, referencing visual motion processing to the current status of the observer's head [83].

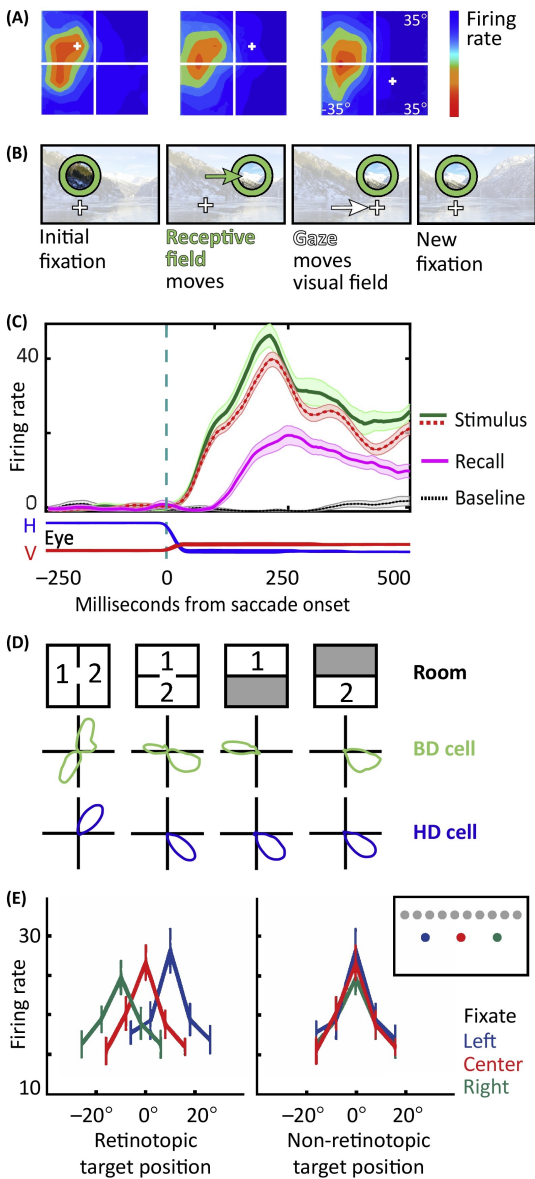


Figure 2: Reference Frame Transformation. (A) Non-retinotopic receptive fields (RF) in monkey parietal cortex. Single-cell rate map of the visual field for three gaze locations (white crosses). RF remains at the same location independent from gaze location (adapted from [63]). (B) Retinotopic updating. Retinotopic RF moves to postsaccadic visual field location before saccade is executed. Adapted from [64]. (C) Non-retinotopic memory signal in retinotopic neurons in monkey parietal cortex. Trial-averaged single-cell response for trials in which a saccade brings stimulus location into RF (green & red). Neuron responds also when stimulus is not shown in the particular trial (pink). Horizontal (H) and vertical (V) gaze movements depicted. Adapted from [71]. (D) Mixed reference frames in rodent retrosplenial cortex. Polar plots of firing rate versus head direction (HD) in different rooms for exemplary bidirectional (BD) and HD cells. Adapted from [77]. (E) Single-cell responses to visual stimuli (grey dots, upper right panel) at three gaze locations (color-coded). Responses plotted in retinotopic (left panel) and non-retinotopic locations (right panel). Adapted from [82].

The PPC-RSC-MTL pathway is bidirectional, suggesting that the MTL also communicates its world-centered visual representation back to neocortical areas. These top-down signals might modulate neocortical processing and contribute to eye-movement invariant receptive fields and visual stability. One possibility is that the MTL provides gaze controlling areas with spatial information about the visual

field before saccades are executed, helping to guide the shift of receptive fields during retinotopic updating [56, 64]. If so, the MTL could act in concert with other brain areas, such as the superior colliculus, which are known to send saccadic corollary discharge signals to cortical regions via the thalamus [56, 65]. However, deficits in visual stability following MTL lesions have not been previously reported, suggesting that the MTL is unlikely to participate in retinotopic updating directly.

Alternatively (or in addition), the MTL may play an important role in transsaccadic memory, an idea at the center of a longstanding debate [84–86] in which the MTL has been largely overlooked. Specifically, the MTL could give rise to a world-centered memory signal that modulates retinotopic neurons [71, 87] (Figure 2C) even after a saccade landed (see e.g., [71, 84–86] for related discussion). Unlike presaccadic retinotopic updating, this MTL world-centered memory trace could be integrated with postsaccadic visual input, providing an efficient (i.e., no active compensation for self-motion required) and noise-resilient (i.e., externally anchored and robust to error accumulation) recalibrating mechanism that could be employed as needed. Areas such as PPC [71] or frontal eye fields [87] could match postsaccadic visual input to the eye-movement invariant visual field representation maintained in the MTL. For example, for each new fixation onset, the self-centered location at which salient visual information occurs could be compared with the MTL’s world-centered map of visual space. Once a correspondence between the self- and world-centered locations is found, the vector that encodes the receptive field shift required to recalibrate the self-centered representation could be fed back to the cortex. The entorhinal grid system has been implicated in this type of vector computation [88, 89]. This proposal does not predict that individuals with MTL lesions have visual stability deficits, since retinotopic updating remains intact, but rather predicts that such individuals should have an increased sensitivity to visual localization error accumulation across saccades. To be useful for such a recalibration process, a maplike memory of the visual field must be maintained in the MTL for at least the time intervals relevant for working memory, a time scale on which the HF does indeed maintain visual memory, as demonstrated by several hippocampal lesion studies (e.g., [35, 90–92]).

Box 2. Anatomy of neocortical–hippocampal interactions in vision

A concept guiding vision science for several decades is the dichotomous organization of the visual system into two major multisynaptic pathways, the dorsal and ventral visual stream. Here, we want to emphasize that these pathways, thought to mediate different aspects of vision, both converge on the MTL in the primate brain [93].

A key processing and relay station of the dorsal occipitoparietal stream is the inferior parietal lobule [93]. It connects not only many parietal, temporal, and occipital regions involved in visuospatial processing, sensory-motor integration, and action planning (e.g., lateral and ventral intraparietal areas, areas V6 and V6A, and the MT+ motion complex [66], but also projects to the gaze-controlling frontal eye fields (FEF) [94] as well as directly and via RSC [95] to CA1 [96] and subicular [97], parahippocampal, and entorhinal cortices [98,99]. Parietal cortex is involved in integrating visual input with gaze movements [63,64] in concert with the FEF [94] and is directly, as well as via FEF and the thalamus, connected to the superior colliculus [56], which is thought to be the prime source or relay station for gaze-related efference copies [56,65]. Thus, this dorsal pathway is most suited to provide the MTL with gaze- and self-motion information.

By contrast, ventral visual areas support visual representations that are invariant to eye movements [100]. The ventral visual stream is a strongly recursively connected network, spanning from early visual cortex via areas V4 and the MT+ [101], inferotemporal areas TEO and TE [102], and RSC [95] to the most anterior parts of the inferior temporal lobe and the HF [103]. It processes information predominantly related to object quality and is thought to extract perceptually relevant features from visual scenes [104], irrespective of their location. However, recent work has found information about locations of visual objects in higher-order ventral visual regions [105], raising the possibility that the ventral pathway provides visual positional information to the MTL as well.

The MTL is hence a convergence zone for visual information in the brain. How might the MTL in turn shape neocortical processing and guide behavior? The key mediator of cortico-hippocampal interactions is the EC [98,99], receiving strong hippocampal input via subicular cortices [97] and projecting to many regions on frontal, temporal, and parietal cortices [106], as well as the RSC [95,107]. The latter is a likely mediator between visual and mediotemporal processing given its strong connectivity to the neocortex. In sum, connectivity suggests strong interactions between visual and mediotemporal systems, putting the hippocampal formation at a key position to shape vision.

0.5 Recall and planning

Like navigation, a key function of visual exploration is to acquire new information about the world. The relationship between viewing and memory (reviewed by [108–110]) is typically examined in image recognition tasks, in which sequences of pictures are presented while humans or monkeys indicate whether they have or have not seen these pictures before. Viewing behavior differs between later remembered and forgotten images, with the number [111, 112] and duration [111] of fixations linked to successful memory encoding. Hippocampal activity directly depends on and predicts visual sampling, even for images that were not consciously remembered [113, 114] (Figure 3A), suggesting that the timing of hippocampal mnemonic processing is tightly linked to visual exploration. Indeed, the timing of saccades themselves is not random but phase-locked to neural oscillations in visual and MTL areas during successful memory encoding [115] (Figure 3B).

Gaze movements interrupt the flow of incoming visual information, prompting the HF to switch between active and inactive encoding states around the time of saccades. The switch between encoding states may be driven by a phase-reset of the hippocampal theta rhythm [116, 117] (Figure 3C), anticipating new incoming sensory information whose encoding depends on a precise interplay between hippocampal spikes and theta phase [118]. Theta rhythms are also critical for grid cell activity during navigation, which lose spatial periodicity when theta is inhibited [119, 120], and for place cells during navigation that fire at specific phases of a theta cycle [121]. While the precise functional role of neural oscillations in the MTL is not yet fully understood [122], they clearly play a critical role in both visual and navigational domains.

Importantly, the relationship between viewing and memory is not unidirectional; what we remember also directly influences how we explore the world (for review see e.g., [110]). Once an image has been memorized, it is less visually explored when it is repeated than when it is novel [18, 123, 124], a change in viewing behavior that depends on the hippocampus [123, 125]. Further, when participants were asked to recall images they had seen before, their eyes re-enacted the same movements they showed during encoding, an effect causally connected to the quality of the recalled memory [126].

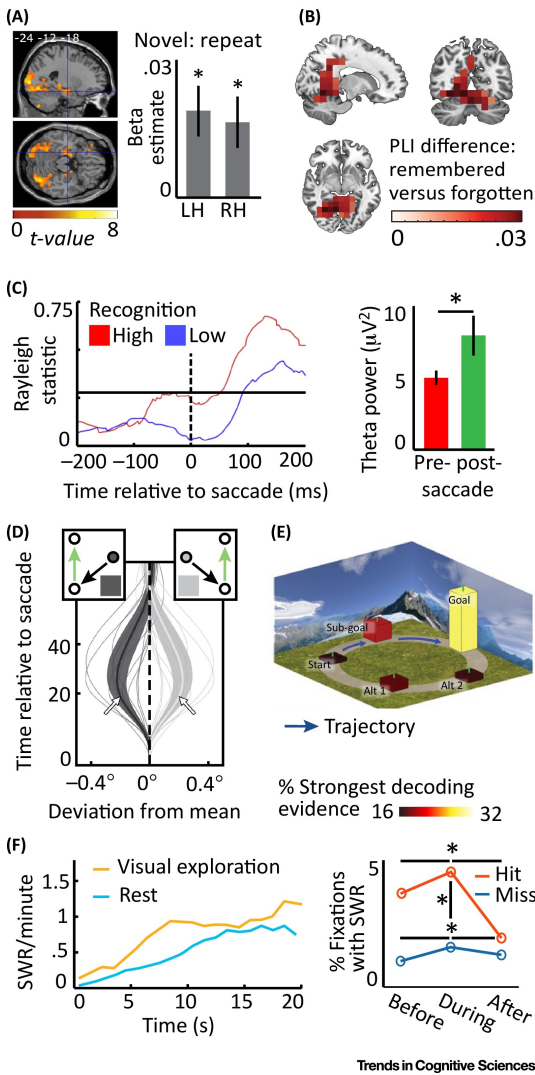


Figure 3: Memory-Guided Planning. (A) Visual sampling of novel images predicts human hippocampal activity. Left: linear parametric modulation (LPM) of number of fixations (t-map threshold $P = 0.005$, 10-voxel extension, uncorrected). Right: LPM is stronger for novel versus repeated images in left (LH) and right (RH) hemispheric hippocampus. Adapted from [114]. (B) Saccades are phase locked to alpha oscillations during successful memory encoding. Phase locking index [across-trial local field potential (LFP), phase-locking index (PLI)] differs significantly between later-remembered and later-forgotten images in human medial temporal lobe. Adapted from [115]. (C) Saccades reset theta phase in monkey hippocampus. Left panel: increase in LFP phase coherence after saccade is higher for high versus low recognition trials. Right panel: theta power increases significantly after saccade. Adapted from [116]. (D) Non-retinotopic carry-over effects in saccade sequences in humans. Second saccade (green arrow in task insets) curves away from first fixation location (adapted from [127]). (E) Navigational route planning in human hippocampus. Decoder trained on goal location and tested on prenavigation planning periods favors subgoals on taken path over those on alternative path. Adapted from [128]. (F) Sharp wave ripples (SWR) during visual exploration in monkey. Left panel: SWR rate increases over time after trial onset. Right panel: SWRs occur more frequently in successful versus unsuccessful visual search trials. Figures adapted from [129].

Such memory-guided viewing has been intensively studied using the ‘inhibition of return’ (IOR) phenomenon, which broadly refers to the fact that after attending to a given visual location, reaction times for returning gaze to that location increase. IOR has been proposed as a novelty-seeking mechanism that maximizes efficiency when exploring a visual scene (for review see [130]). IOR for example has been shown to rely on non-retinotopic visual coordinates [131]. Moreover, when two saccades are performed in a sequence, the non-retinotopic (possibly world-centered) location of the first fixation spot influences the curvature of the subsequent saccade [127] (Figure 3D), suggesting that a top-down non-retinotopic signal influences saccade execution or planning. Such saccade sequences also often have latencies too short to plan and initiate each saccade separately [132,133], requiring the sequence to be preplanned in coordinates invariant to eye movements because all precomputed SDs will have changed after the first saccade [108]. Thus, planning and controlling oculomotor behavior likely requires coordinates referenced to the external world. Since the MTL contributes to goal detection during visual search [134] and contains both a world-centered visual map and SD cells, it is well positioned to perform such computations. In fact, the required computations are similar to those of goal-directed navigational route planning for which the HF is critical [128] (Figure 3E). In rodents, memory-guided route planning during navigation has further been linked to hippocampal sharp-wave ripples [135], which have also been observed in monkeys during visual exploration [129] (Figure 3F), especially when the presented images are repeated [136]. Growing evidence also shows that the same MTL mechanisms guide (or are guided by) the position of visual attention independent of gaze [47, 137]. Together, these results suggest that the MTL drives viewing behavior to efficiently acquire new information about the visual environment [138], in line with the idea that gaze is a behavioral expression of visual predictions [139] generated by the HF [48].

0.6 Context specificity

In addition to encoding a map of the local spatial environment, the hippocampus stores multiple world-centered maps of navigable space (in the ‘cognitive atlas’), allowing it to represent locations in multiple navigational contexts [140]. The ability of the hippocampus to distinguish between contexts during navigation is indexed by remapping, in which contextual changes cause all simultaneously recorded neurons to shift place fields to new locations or stop firing altogether, quickly resulting in a new and distinct spatial representation [141,142] (Figure 4A).

The emergence of remapping depends on several factors, including a navigator's experience with a context [143,144], and can be eliminated by inhibiting hippocampal plasticity [145]. These mnemonic components indicate that remapping facilitates contextual memory during navigation, rather than perceptual processing.

Context also plays an important role in visual tasks by guiding visual search and recognition. In a now standard demonstration of this idea [146], the spatial configuration of an array of distractors in a visual search display provides a unique context that reliably determines the location of a search target. Participants typically find the visual search target faster when they have had prior exposure to the visual context, an effect referred to as 'contextual cueing' [147]. Hippocampal remapping may provide a critical mechanism underlying such visual context effects, by storing multiple maps of visual space (in a 'cognitive picture book') for multiple visual contexts. fMRI studies have shown that contextual cueing is mediated by the hippocampus [148, 149] (Figure 4B), and patients with MTL damage do not show a search benefit for repeated arrays [150–152]. Hippocampal volume correlates with the magnitude of contextual cueing in typical older adults and adults diagnosed with mild cognitive impairment associated with MTL atrophy [153] (Figure 4C). The strength of contextual cueing is modulated by a viewer's experience with the visual context [154, 155], similar to the dependence of remapping on navigational experience [143, 144]. Notably, visual context also modulates fMRI activity in PPC and RSC during search tasks, suggesting that not only world-centered coordinates as reviewed above but also hippocampal context representations may feedback to the broader visuospatial mapping network to guide context-dependent viewing behavior [156].

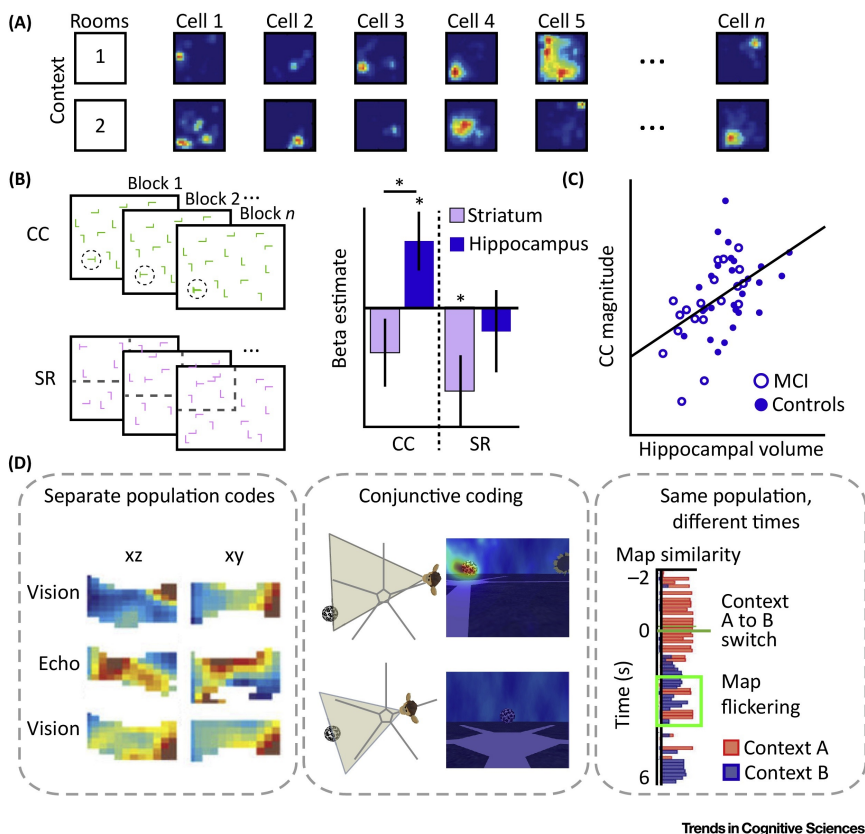


Figure 4: Context Specificity. (A) Hippocampal remapping. Recruitment of a new place cell maps specifically to each navigational context, such as different rooms (adapted from [142]). (B) The hippocampus mediates visual context. Left: participants performed a visual search task during fMRI. Target location was cued either via specific distractor arrangement [contextual cueing (CC)] or probabilistically by stimulus color [stimulus response (SR)]. Right: hippocampus predicted search benefits in CC, the striatum in SR conditions (adapted from [149]). (C) Hippocampal volume correlates with the magnitude of visual contextual cueing (mean response time on novel minus repeated search configurations) in typical humans and patients with mild cognitive impairment (MCI) (adapted from [153]). (D) Three possible hippocampal codes for vision and navigation. Left: same population, different population code. Example: place cells in flying bats remap depending on whether they use vision or echolocation to navigate in the same context (xz is horizontal plane, yz is vertical plane; cell adapted from [157]). Middle: conjunctive coding. Example: monkey hippocampal neurons conjunctively represent gaze- and self-location (example cell adapted from [158, 159]). Right: same population, different time. Example: after one navigational context is rapidly switched to another, rodent hippocampal place cell population spontaneously flickers back-and-forth between representations of the two contexts (map similarity is the correlation between the current population response vector and the average population response vector in context A and B, respectively; adapted from [160]).

The existence of multiple maplike representations in the hippocampus raises three alternatives for how the hippocampus supports maps of both navigational and visual spaces (Figure 4D). First, separate hippocampal populations may mediate representations for the two domains and remap between them depending on their behavioral relevance. In the bat hippocampus, place fields remap depending on whether bats employ vision in light or echolocation in darkness to navigate [157], indicating that, in this case at least, space perceived using different sensory modalities is mapped using separable neural representations. Second, some neurons in the monkey and human hippocampus are sensitive to both body and view location during navigation [158, 161]. Thus, the same hippocampal populations may conjunctively represent navigational and visual spaces. Finally, the same neuronal population may represent both navigational and visual spaces, but at different times, and alternate between visual and navigational maps during simultaneous eye- and body-based movements. Consistent with this idea, the hippocampus ‘flickers’ between representations of two distinct navigational contexts at different theta cycles when there are abrupt shifts in context [160]. Future research using behavioral tasks that require simultaneous monitoring of locations in both visual and navigational spaces are needed to dissociate these alternatives.

0.7 Concluding remarks

It has long been known that vision is important for navigation [162]. However, the converse is less well appreciated. Here we have reviewed mechanisms in the HF that provide the fundamental resource to support several critical computations shared by navigation and vision. We have proposed that the HF, traditionally believed to support navigation, also mediates a world-centered representation of visual space and guides viewing behavior. Since primates are particularly visual creatures, the neural mechanisms that evolved to support navigation in rodents may have been co-opted to support visual exploration as well, leading to strongly intertwined navigational and visual mapping systems. In support of this view, we have drawn on data from both primates and rodents; hence, an important caveat is that we may have elided relevant species differences. The rodent HF mediates representations of non-navigational spaces, such as spaces defined purely by auditory information [163], but whether it mediates a map of visual space is unknown. In primates, visual and navigational mapping systems overlap on a systems level, but whether the two domains are supported by the same neurons remains as yet unknown (see Outstanding Questions).

As a coda, we wish to note our belief that the MTL computations reviewed here likely have broad applications beyond both navigation and vision. The idea that the HF performs domain general computations is not new. Indeed, Tolman originally conceptualized the cognitive map as a heuristic for flexibly guiding behavior in general [164]. Yet, it is only recently that empirical research has begun to take this idea beyond metaphor. We encourage researchers of cognitive domains other than navigation and memory to 'look at' the HF, and further suggest that vision may prove to be the ideal domain for future explorations of how MTL computations support cognition broadly, because visual representations can be characterized concretely in terms of distances and directions in the same way as navigational spaces. By testing whether the same principles govern spatial representations for vision and navigation, and whether the MTL plays the same role in solving analogous problems in both domains, we will have made a key step toward illuminating the function of the MTL in general.

Box 3. Outstanding questions

How, and to what environmental features, are world-centered maps of visual space anchored in a dynamically changing world (e.g., during real-world navigation)?

Do head direction and saccade direction cells play analogous orienting roles in navigation and vision, respectively?

Since visual space does not contain eye movement obstacles in the same way as navigational space, what information drives visual border cells?

Do spatial view and visual grid cells code visual space in depth (e.g., along the ground plane), or only in the two-dimensional visual plane?

Does the MTL world-centered map of visual space support visual constancy (by guiding retinotopic updating or by mediating memory traces of the visual field)?

Is contextual cueing mediated by hippocampal remapping?

Do MTL visual representations drive or are they driven by shifts in visual attention?

Do the same MTL neural populations mediate world-centered representations of visual and navigational spaces (Figure 4C) and how do they interact during navigation?

Do MTL world-centered visual representations emerge in typical development at the same time as world-centered representations of navigational space? Relatedly, do visual representations in the MTL break down along similar trajectories in typical aging and disease as the coding of navigational spaces?

Glossary 1

Border cell: entorhinal or subicular neuron that is active when the animal occupies locations along navigational boundaries, such as walls or cliffs.

Cognitive map: first proposed as mental representation of locations and the relationship between them, cognitive maps are discussed as general map-based coding principle for information in the brain.

Context: spatial, temporal, and situational setting associated with particular behavioral or mnemonic outputs.

Corollary discharge: also known as 'efference copy', it is a copy of a motor command that is sent to the muscles to produce a movement. Sensory areas use corollary discharges to anticipate self-motion related sensory change.

Grid cell: entorhinal neuron that is active when the animal occupies certain locations arranged in a hexagonal lattice, tessellating the environment. Grid cells encode self-location during navigation.

Head direction (HD) cell: neuron that is active when the animal faces into a certain direction in the environment. Head direction cells were found in several brain areas, including the hippocampal formation.

Hippocampal formation: compound of brain regions in the temporal lobe, including the hippocampus proper with its subfields CA1, CA2, and CA3; the dentate gyrus; subicular cortices; as well as the entorhinal cortex.

Non-retinotopic: umbrella term describing representations of visual space that are not retinotopic (see definition 'Retinotopic'). Includes all movement-invariant reference frames, such as world-centered (spatiotopic) and head-centered (cranio-topic) reference.

Place cell: hippocampal neuron that is active when an animal occupies a certain location in the environment. Place cells encode self-location during navigation.

Proprioceptive signal: neural representation of mechanoreceptive information about tendon status and muscle tone. Together with vestibular signals (see definition 'Vestibular signal'), proprioception provides information about position of body parts and movements.

Glossary 2

Retinotopic: retinotopy is the mapping of visual space from the retina to neurons in visual cortex. Here, neighboring visual locations drive neighboring cells. Retinotopic maps are self-centered (see definition 'Self-centered reference').

Saccade direction (SD) cell: saccade direction cell; neuron that is active when the eyes move into a certain direction.

Self-centered reference: coordinate system referenced to one's own body, or parts of it, such as the eye (see definition 'Retinotopy'). Also known as 'egocentric'.

Spatial view cell: hippocampal neuron that is active when an animal looks at a certain location in the environment. Spatial view cells encode gaze location during visual exploration.

Transsaccadic memory: visual short-term memory representation of the presaccadic visual field that influences postsaccadic processing. Transsaccadic memory is discussed as one of multiple mechanisms mediating perceptual stability.

Vestibular signal: neural representation of sensory information about head/body movements relative to the axis of gravity. Vestibular information constitutes an important cue about self-motion and body position in space.

Visual border cells: entorhinal neuron that is active when the animal looks at locations close to the edge of a visual stimulus display. Does not respond to edges within the display.

Visual grid cell: entorhinal neuron that is active when the animal looks at or attends to certain locations in the visual scene. Its receptive fields are arranged in a hexagonal lattice, tessellating visual space. Visual grid cells encode gaze location during visual exploration.

Visual exploration: behavioral strategy to explore the environment by means of eye movements and viewing without the need of navigating, hence without physically moving through the environment.

World-centered reference: self-motion invariant coordinates referenced to external cues such as landmarks or visual features in a scene. Also known as 'allocentric'. Also see the definition of 'Non-retinotopic'.

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