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Trends in Cognitive Sciences

Review

The Versatile Wayfinder: Prefrontal Contributions to Spatial Navigation

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The prefrontal cortex (PFC) supports decision-making, goal tracking, and planning. Spatial navigation is a behavior that taxes these cognitive processes, yet the role of the PFC in models of navigation has been largely overlooked. In humans, activity in dorsolateral PFC (dlPFC) and ventrolateral PFC (vlPFC) during detours, reveal a role in inhibition and replanning. Dorsal anterior cingulate cortex (dACC) is implicated in planning and spontaneous internally-generated changes of route. Orbitofrontal cortex (OFC) integrates representations of the environment with the value of actions, providing a 'map' of possible decisions. In rodents, medial frontal areas interact with hippocampus during spatial decisions and switching between navigation strategies. In reviewing these advances, we provide a framework for how different prefrontal regions may contribute to different stages of navigation.

Highlights

Navigation is a behavior fundamental to all mobile animals, and incorporates various cognitive functions, including memory, planning, decision-making, and updating models of the world.

Historically, the neural underpinnings of flexible navigation have focused on the hippocampal formation, but recent evidence suggests that regions of the prefrontal cortex (PFC) are crucial to many aspects of navigation, especially when environments are complex or dynamic.

This review summarizes what we know from recent human, non-human primate, and rodent studies, proposing a novel perspective that incorporates our knowledge across species and brain regions seeking to avoid tunnel vision in understanding the multifaceted behavior in navigation.

Prefrontal Cortex: An Overlooked Key Brain Region for Navigation

Our planet offers a dazzling variety of environments that animals must navigate. For mammals, a set of four key brain regions are thought to form a core navigation network: the hippocampus, parahippocampus, retrosplenial cortex, and posterior parietal cortex [1,2]. These regions support place learning and flexible navigation requiring self-localization (e.g., 'where am I on this mountain?'). They are accompanied by the striatum for navigation based on actions linked to specific stimuli [3,4] (e.g., 'turn left at the waterfall'). Here, we review evidence that the prefrontal cortex (PFC) is an overlooked key component of the mammalian navigation system which allows the navigator to adapt to changes in the environment, track progress, and plan ahead to avoid making costly mistakes.

Planning, decision-making, prospective memory, goal-coding, and adaptive behavior are all cognitive functions synonymous with PFC function [5,6] and are often required in real-world navigation [1,2]. Indeed, many functional neuroimaging studies have reported PFC activation during navigation [7–22] (Figure 1). So why has the PFC been neglected in theories of navigation? We suggest three main reasons. First, patients with frontal lobe damage are commonly reported to have impaired executive function [23], with navigation impairments being a corollary of a more general dysfunction in the regulation of behavior [24,25]. Second, while brain regions in the core navigation network display spatial coding in their activity patterns, such as **grid cells** (see Glossary) and **place cells** [26], similar coding has been only recently reported for PFC neurons [27,28]. Third, lesions to the rodent medial PFC (mPFC), which receives hippocampal afferents [29], have generally been reported to have little or no impact on navigation in a widely used assay for navigation: the Morris water-maze [30,31]. These observations may explain why many reviews of navigation make little or no mention of the PFC [32–37].

More recent research has revealed that the PFC may play important roles in navigation. Rodent lesion studies have implicated medial PFC regions, infralimbic (IL) and prelimbic (PL) in aspects of navigation, such as learning multiregion environments [38], reversal learning in the water maze [39], and strategy switching [40]. Evidence of spatial metric coding in PFC has been

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reported in rodent [41] and human studies using both functional imaging [42] and intracranial recordings [27,28,43]. Such studies add weight to the argument that PFC is a key brain region for spatial coding in navigation. More broadly, PFC regions may aid navigation by processing the presence of others in the environment to infer popular routes or problems ahead: the social aspects of wayfinding [44]. Consistent with this, the rostral mPFC [45] and anterior cingulate cortex (ACC) [46] are both active when tracking others in the environment, and medial regions of PFC are active when mapping social networks [47] or processing the intentions of others during navigation [48].

Here we integrate findings from humans, non-human primates, and rodents. This cross-species integration requires acknowledgement of the challenge due to the differences in neuroanatomy [49–51], navigation tasks used, and neural recording methods employed. For human studies, overlap in the nomenclature for similar regions can be confusing (Figure 2 and Table 1). It is important not to oversimplify the PFC as a set of separate 'modules', rather it should be considered part of an interconnected set of brain regions, within which the PFC provides a dynamic, state dependent, contribution to network operations via functional networks interacting on both local and global hierarchical architectures [37,52]. However, because of the gaps in our current knowledge, we will often be discussing specific prefrontal areas and their involvement in a specific scenario during navigation.

To examine how different PFC regions might contribute to solving the changing demands imposed by real-world navigation, we draw on the literature to describe how PFC dynamics likely operate during an exemplar navigational journey. Because navigation ability and strategy choices vary considerably in humans [53–56] and other mammals [57], we focus on brain dynamics in successful navigators who efficiently make use of the core navigation network during navigation [18,58].

Selecting the Goal and Making a Plan

We start our navigational journey by setting a goal or goals. Sometimes there is a clear goal, such as 'how do I get home?'. Other times, we may need to select a navigation goal from a set of possibilities, such as 'where can I find coffee in a hurry?'. A trip could range from involving a single familiar goal to multiple new goals. Importantly, navigating a highly familiar route will likely place little demand on PFC or indeed much of the core network for navigation [18,58]. By contrast, selecting a goal from competitors, navigating a novel region of space, or considering alternate routes, would all likely place demands on PFC. Such goal selection and comparison of alternative paths are core example of what defines planning as opposed to the moment-to-moment decision-making at waypoints [8,59–62].

Some models of navigation argue that the PFC supports initial planning [63,64] and distance to goal coding [65] by interacting with hippocampal networks to support navigational guidance [25,62]. Consistent with this, multiple lines of empirical evidence from tasks requiring learning stimulus–reward associations suggest that choosing the correct target from a set of competing alternatives involves the ACC and ventromedial (vm) PFC [66,67]. ACC might integrate the physical demands of travel to guide actions [68,69] and vmPFC might weight alternatives in terms of their potential value [67]. However, there has been surprisingly little research to verify this for navigation. Once the goal is set it may need to be visualized to aid consideration of the route [70]. vmPFC may also play a role in driving the construction of scene imagery of the goal in posterior regions including the hippocampus [71–73], with such scene imagery forming an important part of planning complex routes [70].

Sometimes we must navigate to a set of goals, which requires the allocation of a final goal and subgoals [74]. The neuropsychological task the 'Zoo Map Test' [75], probes the ability to plan

Glossary

Cognitive map: a theoretical construct describing the neural representation that underlies our ability to remember the layout of the environment and store information about events occurring in places.
Default-mode network (DMN): a set of brain regions, including the medial prefrontal cortex, hippocampus, and precuneus/posterior cingulate cortex, which are more active when thought is directed internally, as opposed to towards the external environment.
Grid cell: a location-modulated neuron that fires at regular intervals as an animal navigates an open area. Grid cells have been most commonly found in the entorhinal cortex and are thought to form an essential part of the brain's navigation system by allowing it to understand its position in space by storing and integrating information about location, distance, and direction.
Hidden states: a collection of information relevant to a given decision that is difficult to distinguish based on sensory input alone and is therefore 'hidden'.
Place cell: neurons that become active when an animal enters a particular location within an environment, which are most commonly reported in the hippocampus.
Replay: during 'replay', temporally compressed sequences of place cells reactivate spatial trajectories in explored environments in either forward or reverse order. Replay is associated with high-frequency sharp-wave ripple (SWR) events prevalent during offline periods in both sleep and nonexploratory waking states ('awake replay').
State space: the set of all possible states of the environment that are relevant for a given task, which for navigation might be the possible paths or enclosed spaces available to navigate.
Vicarious trial and error (VTE): a behaviour considered an overt marker of 'mental planning/exploration' or deliberation, observed in rodents at a choice point in a maze, where it frequently pauses and alternately faces towards its potential goal, before deciding.

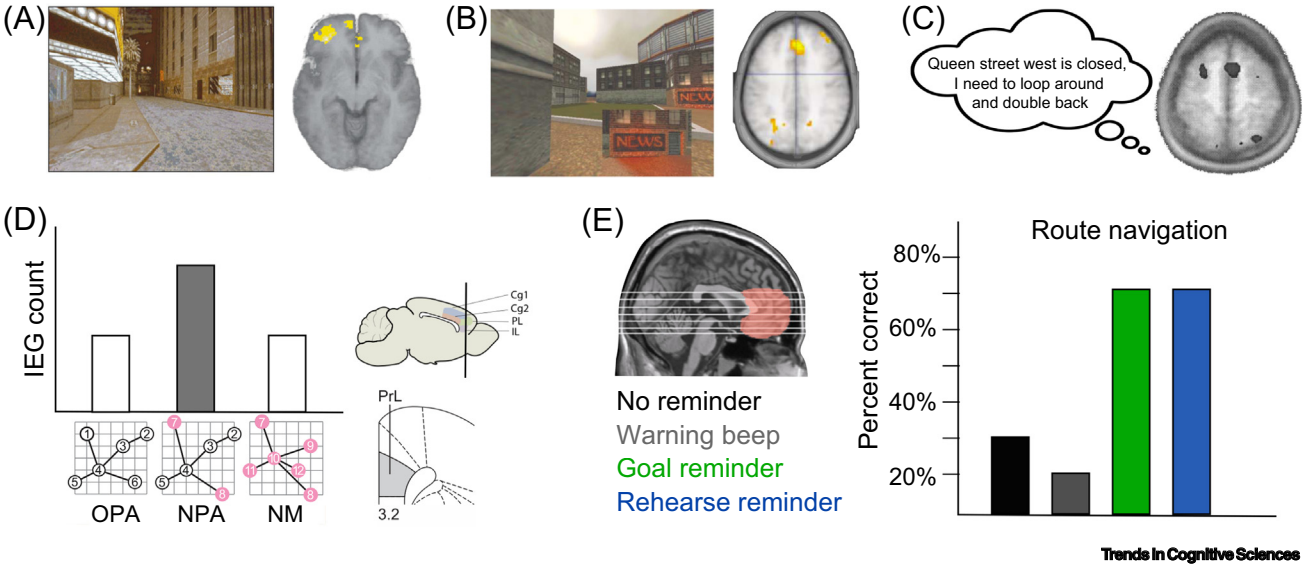

Figure 1. The Prefrontal Cortex (PFC) Is Active During Navigation. (A) Earliest study to show increased PFC during virtual navigation. Activity in the middle and superior frontal gyrus (SFG) is increased when navigating to a learned goal in a virtual town where novel barriers forced detours to the goal. Data from [17]. (B) Increased activity in medial, ventrolateral, dorsolateral, and right anterior prefrontal cortices during wayfinding to goals compared with following a well-learned route to a goal [18]. (C) Middle and left SFG were more active when participants thought about the route around a blocked path in their hometown [123]. (D) Prelimbic cortex (PrL), a proposed rodent analogue of part of human PFC, shows increased immediate early gene (IEG) counts when animals must integrate new memories into an existing spatial memory schema [New Paired Associates (NPA)], compared with when they navigate to learned ('old') object locations [Old Paired Associates (OPA)] or form new maps of the space [New Map (NM)]. An example rodent brain (from [50]) shown with vertical slice indicating location of PrL and exact slice location are shown [141]. (E) Human neuropsychological study in which a patient with ventromedial prefrontal damage was able to find his way between two locations in his hometown if he was given reminders (either of the goal location itself, or a prompt to rehearse the location), but not when no reminders were given or a meaningless reminder was given (a warning beep), pointing to a role of the vmPFC in maintaining the goal in mind while wayfinding [103]. Abbreviations: Cg, cingulate area; IL, infralimbic; PL, prelimbic; vmPFC, ventromedial PFC.

a multistep route from viewing a map and is impaired by medial frontal damage in humans [76]. Single unit recordings in non-human primates indicate that lateral PFC (lPFC) regions code information about multiple step decisions during action planning in on-screen mazes [77,78] (Figure 3E). This research, combined with evidence from nonspatial studies, suggests the lPFC, and its interaction with posterior parietal cortex, is important for planning routes and dealing with subgoals [79], and is necessary for sequencing higher-order behavior [80]. Consistent with this, London taxi drivers making an initial plan for complex routes through London (UK) show increased activity in lPFC regions [21].

lPFC is not the only region engaged during sequential planning. Manipulating the complexity and difficulty of the maze being navigated reveals that rostrodorsal medial (rdm) PFC is more active when decisions are easy at a first choice point but hard at a second choice point whereas dorsal-ACC/presupplemental motor area activity is increased when choices are difficult in general [14]. Lateral frontopolar cortex (lFPC) responded to the difficulty at the second choice point [i.e., future demands only (Table 1, Figure 3B)]. Follow-up psychophysiological interaction analyses showed that coupling between the hippocampus and rdmPFC increased during sequential planning and when correct (versus incorrect) choices were made.

A key question is how might a 'plan' be processed at the neural level? There has been increasing evidence that during periods of relative immobility, sequential **replay** of hippocampal place cells along a future route, whether previously experienced or not, might form the basis for such planning (Box 1) [81–85]. 'Forward sweeps' through alternative future paths have been observed during active movements [86,87]. While these pre/replay events have been extensively studied in

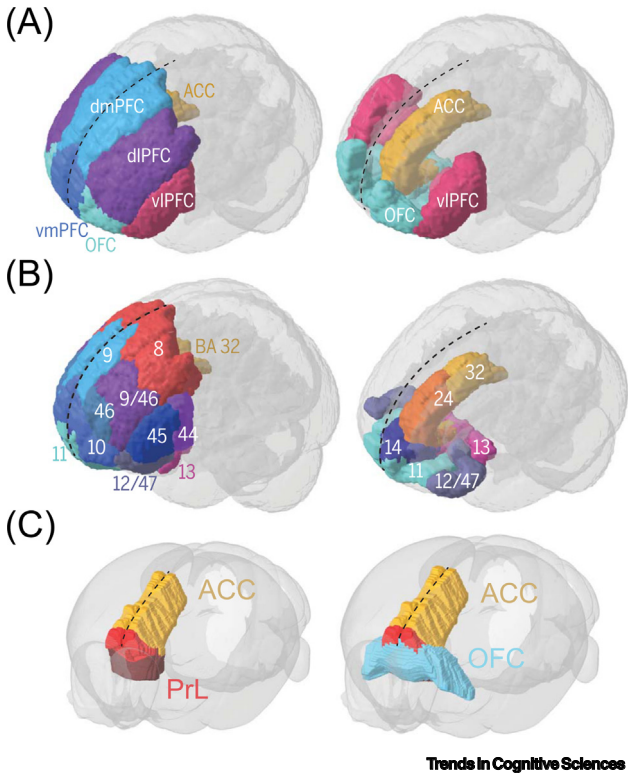

Figure 2. Anatomical Summary and Different Nomenclatures. (A) Functional definition of brain areas (human). (B) Broadman areas (BAs) in the human frontal cortex. (C) Functional definition of brain areas (rodent). Abbreviations: (d)ACC, (dorsal) anterior cingulate cortex [also used in rodent literature, better referred to as (midcingulate cortex) MCC, see [50]]; dlPFC, dorsolateral PFC; dmPFC, dorsal medial prefrontal cortex; lefl lPFC, left lateral prefrontal cortex; OFC, orbitofrontal cortex (also used in rodent literature); PrL(PL), prelimbic cortex (rodent, often also termed 'mPFC' or 'ACC', see [50]); rlPFC, right lateral prefrontal cortex; SFG/rdmPFC, superior frontal gyrus/rostrodorsal medial prefrontal cortex; vlPFC, ventrolateral PFC; vmPFC, ventral medial prefrontal cortex. Reproduced with permission [156].

the rodent hippocampal formation, spatiotemporal reinstatement ('replay') of abstract states has been reported in humans using noninvasive imaging [88,89], and research with rodents has found increased coordinated forward replay across hippocampus and PFC resulted in better spatial memory performance [90], for a review see [60]. Evidence for prefrontal and hippocampal coherence, primarily in the theta band, has also been found in human neuroimaging experiments testing planning with the recall of the spatial location of a target [91] and imaginary future thinking [92].

Travelling: Tracking Progress, Goal Maintenance, and the Default-Mode Network

During navigation, a major part of the journey will likely be simply travelling to the next waypoint or goal [70]. During such travel there is potential for freeing up systems from navigational deliberation for other tasks, such as recalling memories, enjoying the view, mulling future life plans, and general mind wandering [70]. In a recent study we found evidence of increased activity in core regions of the **default-mode network** (**DMN**), including the vmPFC, when periods of ongoing travel through the environment were compared with events where the participants decided to change their plan [13]. Given its proposed role in internalized thought, this may point to a role of the DMN during navigation when no updates need to be made and the route-plan is being followed from memory [59]. Thus, during travel periods in a familiar environment, much of the time may be spent engaging regions of our DMN, possibly due to mind-wandering or the recall of spatial locations along our route [70]. Simultaneous fMRI and intracranial recordings in anaesthetized primates have shown that hippocampal sharp-wave ripples (SWRs), which are associated with place cell replay and memory consolidation in sleep, increase the activation of the cortical DMN [93]. However, it is unclear how planning indexed via hippocampal replay events interact with the DMN during active navigation. Moreover, PFC dynamics based on spontaneous behavior are missing in most models of navigation. This may be because most studies are

Table 1. Variety of Functions Associated with the Prefrontal Cortex in the Context of Navigation Behavior

Brain region[a]	Function	Refs
ACC/*PL*	Effort	[69]
	Grid coding of space	[27]
	Recalling episodic memories of the environment	[147]
	Vicarious trial and error behavior	[112]
dACC/*MCC (midcingulate cortex)*	Hierarchical coding	[8]
	Difficulty of choice (current and future)	[14]
	Inhibition of current plans	[12,13]
	Predictive monitoring of the environment and the agents moving in the environment	[105]
	Backtracking	[13]
	Foraging/counterfactuals	[133]
Frontopolar cortex (BA10)	Future choice	[14]
	Searching possible paths in future	[11,52,137]
mPFC	Proximity to the goal	[16,22]
	Replay	[151]
	Path integration	[152]
OFC	Proximity to the goal	[74]
	Determining the decision/state space	[115]
	Grid cells	[153]
	Regret	[154]
SFG/(r)dmPFC (BA8)	Difficulty of choice (current to future, Interaction); coupling with hippocampus increased when correct choice	[14]
	Novelty detection and environmental changes leading to replanning (e.g., long detours)	[12,25]
	Path integration (reducing error)	[102]
Right lPFC (vlPFC)	Novelty detection and environmental changes leading to replanning (in particular long detours and false shortcuts, but not real shortcuts)	[12,25]
Left lPFC (vlPFC)	Difficulty of future choice	[14]
vmPFC	Optimizing search path	[155]
	Scene construction	[73]
	Integration with existing schema	[39,141]
	Maintaining current goal	[103]
	Grid-coding	[42,153]

[a]Human-centric organization; italics refer to the structure in the rodent brain; see Figure 2 in the main text for more details on nomenclature used.

optimized to include as much time as possible focused on navigational processing. Future research integrating across rodents and humans with longer more diverse experiences may be useful.

Sometimes however, we cannot be on 'auto-pilot' and choices are needed to reach our destination. While reports of 'goal' related activity have mainly focused on the rodent and human hippocampus [83,94,95], there is ample evidence of a similar signal in mPFCs [41,96,97]. In a seminal study, Ekstrom *et al.* [28] recorded neurons of presurgical epileptic patients navigating a virtual

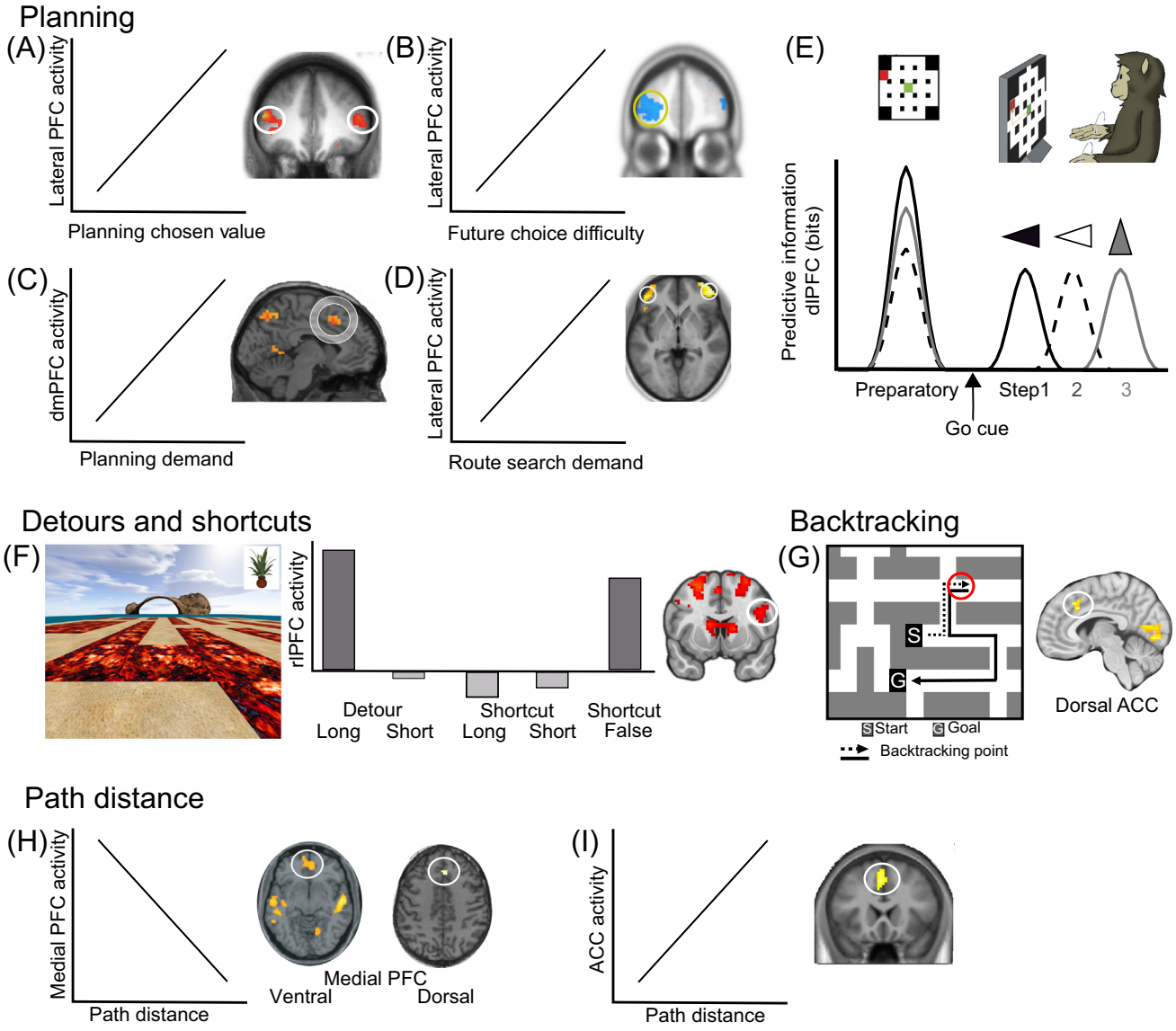

Figure 3. Examples of Prefrontal Activity to Specific Events During Navigation. Neural activity changes as a function of the behavioral correlate are represented by the schematic. Route planning has been shown to involve responses in prefrontal cortex in (A) an unstable ever-changing environment [15] , a simplified maze [14] , (B) film simulation of a real city [10] , (C) a virtual subway network [8] , and (D) a virtual render of a city [21]. (E) Macaques performed a multistep maze task and before the onset of movement, all future actions (three cursor motions) within the maze were selectively encoded in the population firing rate of dorsolateral PFC (dlPFC) [Broadman area 46 (BA46)]. These neurons did not code for the physical actions (arm movements) that were decoupled from the steps within the maze [77]. (F) View in a virtual desert island, in which shifting paths of lava create shortcuts and detours to hidden treasure [18]. Activity in superior frontal gyrus and right lateral prefrontal cortex (rlPFC) is increased when detours adding a larger distance to the route were compared with detours adding a short distance. Importantly rlPFC was also activated by false shortcuts (i.e., changes in route options that seem like a shortcut but will in fact lead the participant away from the goal [12]) . (G) Dorsal anterior cingulate cortex (dACC) was active when participants engaged in 'backtracking' (i.e., voluntarily changing their path) (inset shows an example of such a backtracking event overlaid on a portion of the maze from (F) (white: walkable paths; gray: path boundaries) [13]. (H) The medial prefrontal cortex (medial PFC) codes path distance to the goal location during initial planning [16] and during travel periods [22]. (I) The anterior cingulate cortex (ACC) codes path distance during travel periods [10] . Abbreviation: dmPFC, dorsomedial PFC.

environment and found frontal neurons, which were selectively active for specific goal locations and maintained their activity during the travel. This work was recently extended by showing goal selective activity in mPFC regions, revealing the oscillatory dynamics of such regions for

Box 1. The Role of Prefrontal–Hippocampal Interactions in Navigation

Evidence supports the idea that prefrontal cortex (PFC)–hippocampus engage in coordinated activity [143–145], and in fact point to the role of the PFC in driving hippocampal activity in certain situations when the goal states (e.g., current target) need to be retrieved in a context appropriate manner [109,147,148]. The importance of PFC and medial temporal interaction has long been established for memory processes such as encoding and retrieval [6] and for incorporating new information into existing memories or schemas [140], for example, via immediate early genes that are activated in the prelimbic cortex of the PFC during hippocampal-dependent memory encoding [141,149]. Simultaneous recordings from the anterior cingulate cortex (ACC) and CA1 in the rodent has also shown that during remote recall the ACC drives hippocampal activity to increase representations of context to facilitate retrieval [147]. One conclusion that follows is that PFC may be important for reducing interference during hippocampal dependent tasks such as navigation. Further supporting this view, it has been found that increased medial PFC (mPFC)–hippocampal synchrony resulted in less interference from the previous learned rule in a spatial task requiring rule switching [40]. Crucially the mPFC was not important for initial learning and retrieval, only for the maintenance of rule reversals, and was shown to precede activity in CA1 during early stages of learning, and also when this learning was rapid. This new evidence suggests that the PFC may have a role in facilitating this rule switching process, or even initiating it [147]. Similarly, during early learning of rules concerning reward locations on a simple W-shaped maze, PFC to CA1 spiking synchrony was increased, even higher than during sleep [150]. For further reviews on PFC–hippocampus interactions see [59,60,62].

coding information for navigation [43]. The representation of salient locations has also been found in the rodent PL area, and these cells outnumbered 'place' cells found in the same region that code for current location [41,95]. Goal trajectory information appears to be conveyed from the rodent mPFC to the CA1 region of the hippocampus via the nucleus reuniens (NR) once learning is established, but this interaction is reversed during early learning [98]. While these studies show the representation of general goal coding or sequences [99] or paths to a goal [100], they do not explicitly show the coding of the specific, current goal location. It is also unclear whether goal-coding observed in hippocampal regions is inherited from PFC regions or vice versa. Evidence suggests that the core spatial computations for distance, direction, and future trajectory come from the hippocampal formation, but that computations supporting goal selection and other aspects of navigation covered in this review likely arise in the PFC, which exert influence on the spatial computations in the hippocampal formation.

In humans, dorsomedial PFC (dmPFC) may track progress to the goal. dmPFC showed increased activity during periods of travel where the navigator reported looking ahead for a key landmark or junction [48], and when keeping track of self-motion relative to a previous location [101,102]. Activity in the mPFC scales with current goal distance in both lifelike route planning [8,10,22] and in simplified environments [20,74] (Figure 3H). In a rare case, a patient with extensive vmPFC damage was tested on real-world navigation of a familiar environment and was found to frequently forget the current goal and arrive instead at locations that were very familiar. If the patient was given reminders to maintain the goal, they were able to navigate successfully (Figure 1E), indicating that ventral regions of the PFC may play a key role in goal maintenance during travel, rather than long-term memory for the goals [24,103]. This observation may also relate to neural activity recorded in similar regions in non-human primates, where progress (proximity to reward) through a set of sequential stimuli was found to be tracked by increasing activity in ACC [104]. When monkeys were tasked with moving a cursor to capture a virtual prey on a 2D computer display, dACC neurons were found to predict the future location of a target [105]. This not only extends the finding that the PFC is involved in predicting future states, but also indicates that it can represent an external entity. It should be noted that goal distance tracking can be confounded by a number of other spatial factors, such as the number of upcoming choices and proximity to reward [83]. Furthermore, recent evidence in rodents suggests the PFC may not purely support maintenance of the current goal location [106].

Choosing the Correct Path at Waypoints

For many terrestrial animals, navigation often occurs along distinct paths due the vegetation, rock formations, or the structure of urban developments. A key challenge facing the navigator is

choosing the optimal path when confronted with options. Increased dlPFC activity is evident when navigators are making an active choice compared with when their choice is guided at junctions [10,58]. Sometimes it may be difficult to choose the path because the two options ahead have a similar distance to the goal. dlPFC, vlPFC, and ACC activity in humans has been reported to increase with the similarity of the distance between the alternative paths to a goal [16]. In rodents, a number of studies have shown that during active navigational decision-making PFC–hippocampal interactions increase (e.g., phase-locking of firing or increased coherence in local field potentials [107,108]). Recent evidence suggests CA1 can share future goal information with mPFC and that mPFC may guide which goal is coded by CA1 [109].

One striking piece of evidence for path choice behavior in rodents comes from Muenzinger [157], who described back-and-forth looking behaviour at choice points in a maze. This **vicarious trial and error** (**VTE**) behavior resembles 'planning' in animals when there is uncertainty, and has been shown to be hippocampal dependent [110] and inversely related to replay linked hippocampal SWRs [111]. VTE is thought to rely on hippocampal–cortical interactions [61], and recent evidence suggests that disruption of the dmPFC reduces VTE behavior and has downstream consequences in the hippocampus [112], pointing to a more direct role in planning during memory-guided behavior. Consistent with a role in coordinating behavior, disruptions to rodent medial PFC also disrupts the capacity to switch between place and response strategies at junctions in a maze [40].

In terms of evaluating choices, the orbitofrontal cortex (OFC) has been argued to operate as a **cognitive map** of the **state space** required for value-based decision making, in particular in allowing inferences about **hidden states** and connections [113,114]. Evidence for this so far has been lacking for navigation, but studies exploring choices with nonspatial stimuli in humans support this view [115], including the role of the OFC in representing distant states in the future [116]. A recent study showed that OFC, but not ACC, inactivation in rodents abolished inference-based foraging on a lever-based pressing task and lead to stimulus-bound behavior in a foraging task [117]. Similarly, OFC lesions in rodents cause deficits in choice behavior when action–outcome associations are hidden, but not when they are directly observable [118]. Recent rodent and human evidence suggests that the OFC is involved in updating and learning values, not directly in choice behavior itself [119,120]. Thus, it seems likely that the OFC would play a key role in assigning value to choices at junctions during navigation, via inferences about untaken but possible paths.

Adapting the Plan: Detours and Shortcuts

Despite meticulous planning and keeping the goal in mind, the navigator may still struggle to reach their goal. Detours are a frequent and frustrating part of life. However, animals show a remarkable capacity for adaptation, with the earliest detour behavior reported for spiders in 1912 [121]. How the brain adapts behavior when detours are required has been the focus of a number of human neuroimaging studies. These have consistently reported PFC activity (for a review see [25]). Superior frontal gyrus (SFG) and (predominantly right) lPFC are activated when people encounter detours in their path [10–12,15,16,19,21,122,123], which suggests these regions play a role in halting behavior when unexpected changes in the environment are detected. Such a result is consistent with this area being involved in detecting novelty [124], or updating predictions about the environment with a 'prediction error' [125], and response inhibition [126]. Consistent with this, in a study involving continuous changes in possible paths, activation in lPFC is scaled with the difference between the learned value of a route and its value after the change [15].

Some detours can be a mild inconvenience along a similar length of path, while others can cause significant additional travel. Thus, activations linked to detours may vary in relation to future

demands. To explore this, in a recent study [12], participants navigated a familiar maze in order to find various goal objects. Compared with the training period, however, changes to the previously familiar layout of the maze occurred during the test phase, causing participants to encounter either a block in the path (detour) or a new opening (shortcut). Importantly, both the type (detour or shortcut) and magnitude of change (long or short) were manipulated. Firstly, prefrontal areas increased activation upon the detection of detours only, not shortcuts, and secondly, they were maximally active when a large detour was required (Figure 3F). This points to a specific role of the SFG and right lPFC (rlPFC) in representing prediction errors that increase with demands and when significant rerouting is required, rather than pure novelty. When a detour is encountered, planning the new route may require searching through the possible paths available to reach the goal. Javadi *et al.* [11] found that at detours, lPFC activity increased when the number of future streets to consider was higher (Figure 3D), indicating this region may be performing a breadth-first search through the possible paths.

Few human studies have explored the neural responses during shortcuts [12,15] and even fewer in rodents [127], despite evidence that *de novo* paths, including shortcuts, can be generated in neural responses [84] and Tolman's emphasis on this behavior in his conceptualization of the cognitive map [128]. There is little evidence of evoked increases in PFC activity when novel shortcuts were detected and taken [12]. This highlights that visual changes in the path and changes in the current plan do not necessarily result in observable responses in the PFC. However, increased rlPFC activation was evident when false shortcuts were encountered (a novel path option is encountered that appears to lead to the goal, but actually adds distance). When such false shortcuts were correctly rejected, SFG was active (Figure 3F). This indicates that the rlPFC may be involved in initiating a stop signal driving replan, whereas the SFG is important for processing and successfully resolving conflict between route options [25]. Exploring neural oscillations during navigation revealed decreases in beta power when false shortcuts needed to be avoided [12]. Such reductions in beta power have been associated with increased mnemonic reactivation [129], suggesting a need for increased mnemonic processing of the spatial layout when unhelpful novel paths must be avoided.

Backtracking

Occasionally, it is not the environment that causes a change in route, but rather ourselves when we realize we have taken the wrong path. This can be observed when an animal turns around and 'backtracks' along the path just taken [130]. Only a couple of studies have reported the neural correlates of this process [13,131]. Javadi *et al.* [13] found that during navigation, participants would intermittently backtrack and that in the majority of cases this was the optimal choice (Figure 3G). At the initiation of backtracking dACC was more active and regions associated with the core DMN suppressed. This is consistent with work showing that dACC processes new information linked with uncertainty and updating beliefs or behavior [132], choosing future options [133], increased foraging behavior [67], and the ability to switch and maintain new strategies [134]. The idea that the dACC preferentially represents the value of the 'nondefault' option and the vmPFC represents the value of the 'default' option [135] also dovetails with our result that DMN activity, which includes the vmPFC, was decreased when this spontaneous (and nonstandard) behavior was exhibited. Leveraging the high temporal resolution of magnetoencephalography, it was possible to reveal that 700 ms before the onset of backtracking, alpha power decreased, a pattern of activity associated with anticipatory changes in attention [136]. Thus, the brain may shift between a default state of moving through the environment following external environmental cues, to a focus on internal (memory-based) guidance systems to guide action. Other theories argue the polar frontal cortex should also be engaged for such switches [137]. However, this has not been observed yet during navigation. New evidence shows that activity in

Key Figure

Expected Human Prefrontal Engagement During Navigation

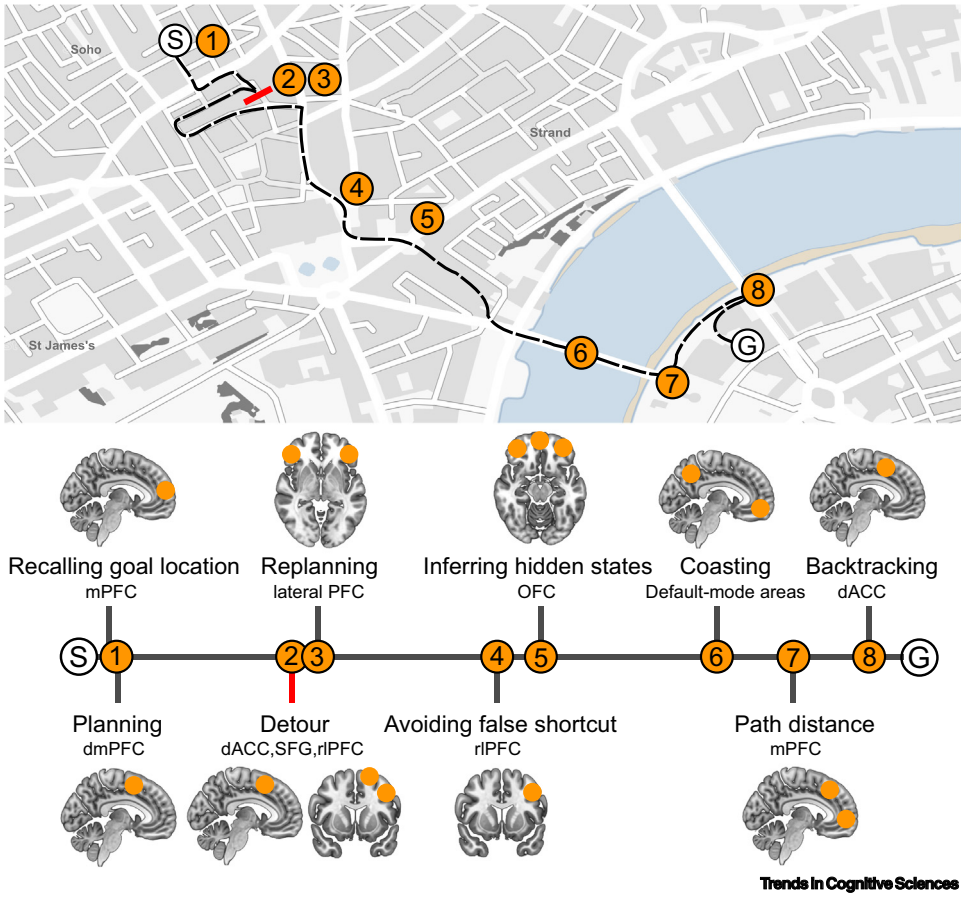

Figure 4. Making a trip from a cozy pub in Soho. London, UK, (S) we first recall where our goal is located, medial PFC (mPFC) interacts with the hippocampus to support recall and mental scene construction of the goal (1). Accessing possible routes and comparing them requires dynamic interactions within dorsomedial PFC (dmPFC)/ dorsal anterior cingulate cortex (dACC) and lateral PFC (lPFC) (1). En route, a barrier is spotted that elicits enhanced activity in the superior frontal gyrus (SFG), right lateral PFC (rlPFC), and dACC, halting the current plan and driving new planning (2). Inferior lPFC supports a search through the different route options to select a new path (3). We encounter a path that appears to provide a potential shortcut to the goal. However, retrieval and simulation of the future route leads to the conclusion that this is a waste of our time, with rlPFC engaged to suppress choosing this path (4). The orbitofrontal cortex (OFC) updates representations of the usefulness of paths (including inferred states for the false shortcut just avoided). OFC activity helps process rule-based state information about what paths are possible when we are walking rather than driving, modulating the affordances of different paths (5). While coasting along the pedestrian bridge, we have no immediate actions to plan or take, so the default-mode network becomes active (6). As we approach the goal region, mPFC and ACC code the path distance to our goal (7). Having gone too far down the riverside walk, dACC activity plays a role in changing the current plan, resulting in backtracking to a previous point in order to correct our route (8). Finally, we arrive at the Hayward Gallery, and enjoy another gin and tonic before experiencing the art (G).

the hippocampus is increased for upcoming attentional states that facilitate spatial-relational processing based on memory-guided cueing, but this is not the case for the mPFC, which predicts attentional states from both memory or explicit cues [138]. Translating this to active wayfinding, it

would be interesting to explore how externally or internally derived attentional cues modify navigation behavior and prefrontal activity. More research exploring how changes in attention impact neural activity in navigation is needed.

Goal Approach and Memory Consolidation via Prefrontal–Hippocampal Interactions

The last step of a journey involves approaching the goal location. In mice, such approach behavior has been related to activation of pathways linking the hippocampus to frontal cortical regions [139]. Evidence suggests arrival at a goal may trigger consolidation of the recent experiences in existing memory networks, particularly if a novel route was required or if the new route is added to a schematic representation of the space [140,141] perhaps allowing meta-learning over multiple experiences [142] and updating a map of the state-space for navigation [115] (Box 1).

Directly linking PFC–hippocampal coordinated activity to measurable outcomes in navigation behavior, a recent rodent study demonstrated two fundamental advancements on this topic: first, coordinated replay between CA1 and PFC was higher for trajectories that were subsequently taken, than for alternative but untaken paths (both for forward and reverse replay events), and second, the strength of this relationship during recall of the task rule also predicted performance on the task [90] (Box 1). This points to a role in PFC–hippocampal interaction, not only in terms of planning, but also for consolidation of successful routes post arrival at the goal [143–145].

Concluding Remarks

We have argued the PFC plays a pivotal role in a range of situations during navigation (Figure 4, Key Figure and Table 1). Such situations include: route planning, adapting to changes in the environment, updating route plans, tracking the goal, choosing paths, and representing their value, and consolidating and abstracting from spatial memories. Future computational models that predict the engagement of PFC subregions during different events in navigation would be highly beneficial. This combined with empirical testing of these models across species with directly comparable tasks may provide a way forward in helping understand the full contributions of the PFC to navigation [146]. We have outlined important questions arising from this review (see Outstanding Questions). These include how different PFC areas interact with regions in the core navigation brain network to support flexible guidance, what neural mechanisms the PFC uses to plan and select navigational goals, and how the PFC tracks information for successful navigation.

Outstanding Questions

How do different PFC regions interact with each other and posterior regions to support navigation? Here we have focused on evoked responses in PFC across different tasks. In future it will be important to create models that predict when different PFC-linked brain networks are engaged for particular situations and computational demands.

To what extent does the role of the PFC during navigation depend on the environmental context (familiar versus novel) and/or the strategy adopted? Only a handful of studies have looked at navigation by directly comparing recently learned versus highly familiar environments, and there is some evidence of prefrontal activity when navigating places well-known to participants. How familiarity of an environment relates to different types of navigation strategies is still unclear.

How can we better integrate results across species? A key challenge in understanding PFC contributions to navigation comes from the differences in PFC anatomy, tasks used to test behavior, and methods employed. With the advancement of virtual reality technologies, we can anticipate more studies that use larger spatial scales, making laboratory tasks more similar to real-world navigation; these also offer the possibility of testing the same paradigm across species with near-identical test conditions, allowing comparison with artificial agents to understand potential mechanisms.

How can we incorporate what we know about PFC function during natural behaviors, such as navigation, to better understand changes occurring in healthy ageing and cognitive decline?

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Declaration of Interests

The authors have no interests to declare.

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