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Where am I and how will I get there from here? A role for posterior parietal cortex in the integration of spatial information and route planning

Jeffrey L. Calton¹ and Jeffrey S. Taube²

¹Department of Psychology, California State University – Sacramento

²Department of Psychological and Brain Sciences, Center for Cognitive Neuroscience, Dartmouth College

Abstract

The ability of an organism to accurately navigate from one place to another requires integration of multiple spatial constructs, including the determination of one's position and direction in space relative to allocentric landmarks, movement velocity, and the perceived location of the goal of the movement. In this review we propose that while limbic areas are important for the sense of spatial orientation, the posterior parietal cortex is responsible for relating this sense with the location of a navigational goal and in formulating a plan to attain it. Hence, the posterior parietal cortex is important for the computation of the correct trajectory or route to be followed while navigating. Prefrontal and motor areas are subsequently responsible for executing the planned movement. Using this theory, we are able to bridge the gap between the rodent and primate literatures by suggesting that the allocentric role of the rodent PPC is largely analogous to the egocentric role typically emphasized in primates, that is, the integration of spatial orientation with potential goals in the planning of goal-directed movements.

This review examines the role the posterior parietal cortex (PPC) plays in spatial orientation and navigation. The successful act of navigation likely requires the integration of a number of different spatial constructs, including location and directional heading, the perception of linear and angular movement, the updating of spatial orientation after movement using idiothetic and landmark cues, and finding one's way along a route – often referred to as wayfinding. We argue that one role of the PPC in this behavior is to integrate the organism's perceived spatial orientation (i.e., the perception of current location and directional heading relative to the immediate surrounding environment) with the overall spatial view of the world (i.e., the spatial relationships of landmarks and goals with one another) in order to formulate an accurate route or trajectory to a goal. To expand on this concept further, consider the process of memory. It is often described as consisting of three major processes: 1) encoding, 2) consolidation, and 3) retrieval. A deficit in any one of these three functions will result in impaired performance on a memory task. Similarly, navigation can be thought of as composed of three processes: 1) spatial orientation, 2) manipulation of spatial representations to enable the computation of a planned route, and 3) execution of the plan. Like memory, a deficit in any one of these processes would result in poor output – in this case inaccurate navigation. In this review we contend that navigational deficits seen after damage to the PPC are largely due to an inability to integrate spatial orientation with the spatial position of the final goal and in formulating a plan to attain

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that goal. In this view, it is thus possible to have a deficit in navigation without an impairment in the individual's perceived spatial orientation.

This view is consistent with a number of observations about the types of spatial deficits experienced by subjects with parietal damage. For example, one of the more well-known parietal disorders is Balint's syndrome – an ataxia where the subject is unable to make an accurate limb movement to a target location (Balint, 1909; Demasio & Benton, 1979; Holmes, 1918). The deficit is usually characterized as an inability to integrate visual spatial information about the target with the necessary motor movements required to attain it. Note, however, that the patient may have a normal perception of their own spatial orientation, and that they can execute a movement to the goal, albeit an inaccurate one. Thus, the deficit appears to lie in understanding the spatial relationships between the body and the target and/or in computing an accurate limb movement from one spatial position to another. In many ways, the problem these patients have is analogous to the navigational deficits seen in rodents with parietal damage, with the primary difference being one of scale. The primate literature has mainly focused on tasks requiring the manipulation of spatial relationships within the personal space of the subject (i.e., Balint's syndrome) (e.g., Buneo & Andersen, 2006; Colby & Goldberg, 1999; Snyder, Grieve, Brotchie, & Andersen, 1998) or the use of functional-imaging techniques with subjects that are stationary and performing a spatial task (Aguirre & D'Esposito, 1997; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003; Maguire, Burgess, Donnett, Frackowiak, Frith, & O'Keefe, 1998; Maguire, Spiers, & O'Keefe, 2001; Merriam, Genovese, & Colby, 2003). In contrast, rodent studies have emphasized tasks on a much larger scale addressing issues of whether an animal can accurately navigate from one location to another (e.g., Parron & Save, 2004; Save, Guazzelli, & Poucet, 2001; Save & Moghaddam, 1996). In both cases, the deficits are similar in the sense that there is an inability to manipulate spatial relationships to formulate a plan to accurately move the body or limb to another place in space. In this review we argue that one of the major roles of the PPC is to perform this integration of spatial information in the planning of goal-directed movements. We will provide further evidence that humans and animals with PPC damage retain the ability to perceive their spatial orientation and execute a movement, but have deficits in understanding the spatial relationships amongst different elements in the environment, which then leads to errors in determining an accurate route to a goal.

Two forms of navigation

Animals appear to use two basic and complementary processes for localization of position and directional heading while navigating. Path integration (also known as dead reckoning) is the process by which current position is estimated by performing an integration of movement velocity (direction and speed of movement) over time since the last known position (Gallistel, 1990; Mittelstaedt & Mittelstadt, 1980). During locomotion, movement velocity can be estimated using self-movement (idiothetic) cues such as vestibular signals of linear and angular head velocity, proprioceptive cues, optic-flow, and motor efference copy. While Darwin (1873) himself hypothesized that animals may navigate in this way, Mittelstaedt and Mittelstadt (1980) provided some of the first documented evidence of this in a mammal, by showing that if gerbil pups are displaced from their nest in total darkness, the mother upon finding them can take a direct route back to the nest in the absence of orienting landmarks, despite taking a meandering path in her outward search. While the idiothetic cues used for path integration are readily available during self-motion, this process does have shortcomings as accuracy is dependent on the continually updated, error free, storage of movement information. Any errors occurring during this process will tend to accumulate, leading to increasingly larger inaccuracies in position estimation over the course of an excursion. A second method of estimating one's position, landmark navigation (also known as piloting or place recognition), relies upon the presence of stable allothetic (landmark) cues in the environment (Gallistel,

1990). Perhaps the best example of this technique in the laboratory is the classic Morris water maze (Morris, 1981), where the animal is placed in a pool of opaque water at random positions and must learn to locate the position of a hidden platform based on the constellation of visual cues in the surrounding room. While landmark navigation would appear to be more accurate than path integration (or at least less prone to error accumulation), the availability of familiar landmarks on a given excursion may be limited, and so a compromise is to use the process of landmark navigation to locate one's position when landmarks are available, and path integration to accurately navigate in the absence of available landmarks.

The Role of Posterior Parietal Cortex in Navigational Behavior

While much attention has been given to the navigational role of subcortical limbic structures and associated limbic cortex, we know much less about the role of the neocortex in this behavior, despite the fact that the sensory and motor signals necessary for path integration and landmark navigation may readily occur there. Clinical case studies have long recognized the importance of the parietal cortex for spatial orientation, as several studies have shown that parietal damage leads to topographic disorientation (De Renzi, 1982; Hublet & Demeurisse, 1992). Similarly, a number of investigators have suggested that the posterior parietal cortex (PPC) may be an important area in the rat neocortex for navigation (Arbib, 1997; McNaughton, Leonard, & Chen, 1989; Save & Poucet, 2000a). The origin of this view mostly arises out of the role of the primate PPC in spatial orientation and subsequent attempts to identify a rat homologue to this area.

In the earliest electrophysiological investigation of the primate PPC, Mountcastle and colleagues described PPC (equivalent to Broadman's areas 5 and 7) as a multisensory area involved in directing attention to and exploration of space close to the body (Mountcastle, Lynch, Georgopoulos, Sakata, & Acuna, 1975). While Ungerleider and Mishkin (1982) considered PPC as visual association cortex, and included it as an element of the dorsal visual stream important for processing the "where" aspect of visual perception, Goodale and Milner (1992) modified this view to the role of processing visually guided actions. Human patients with damage to PPC show deficits such as unilateral neglect and errors in reaching for a visual target (Critchley, 1953), deficits that cannot be described as strictly sensory or motor, but rather a combination of these two functions. In accordance with this, recent conceptualizations of this area in the primate give it an important role in sensory-motor transformation, providing multiple action-specific reference frames from which spatial targets close to the body are transformed into egocentric* coordinates for the planning and/or guidance of movements (Buneo & Andersen, 2006; Colby & Goldberg, 1999; Medendorp, 2008).

Early attempts at characterizing the rat cerebral cortex did so largely on the basis of cytoarchitecture and there was much disagreement as to the extent and location of the associative parietal areas (for a review, see Corwin & Reep, 1998). In one of the earliest descriptions of the rat cortex, Krieg (1946) identified the equivalent of Broadman's area 7 distinct from the more rostral somatosensory cortex and caudal occipital cortex. Subsequent authors either verified (Kolb & Walkey, 1987) or disputed (Chandler, King, Corwin, & Reep, 1992; Zilles & Wree, 1985) the ability to distinguish on cytoarchitectural grounds a true area 7 or PPC from visual association cortex. This lack of anatomical clarity as to the location and extent of rat PPC has led to methodological differences among researchers using a lesion approach to study the function of this area. In localizing their lesion sites most investigators

*Egocentric space is defined by using the organism as the reference frame. In contrast, allocentric space uses the external world as the reference frame. For example, an animal utilizing a rule to always turn right at the choice points in a maze is using an egocentric reference frame while an animal that uses landmarks to guide itself to go north, south, east, or west is using an allocentric reference frame, since these cardinal directions use the external world, and not the organism, as a reference frame.

have used similar coordinates for PPC in the medial-lateral dimension, beginning 1.5-2 mm lateral to the midline and spanning 3-4 mm to the side; however, there are wide variations in the anterior-posterior (AP) placements of PPC lesions across studies. For instance, DiMattia and Kesner (1988) localized PPC as a 4 mm long strip with the rostral border beginning 0.5 mm anterior to Bregma. In contrast, Kolb and Walkey (1987) and Save and Poucet (2000b) used an area of similar dimensions, but marked the rostral border 2 mm posterior to Bregma. Finally, Ward and Brown (1997) utilized a 2 mm long lesion beginning approximately 4 mm behind Bregma. A more recent strategy is to localize PPC on the basis of the unique connections of this area to thalamic and cortical structures (e.g., Corwin & Reep, 1998; Save & Poucet, 2000a). In addition to potentially being less subjective than the earlier cytoarchitectural studies, this approach reinforces the view of PPC as a cross-modal, multisensory area given its abundant connections with other cortical areas.

Despite the methodological differences in the placement of PPC, it is a generally consistent finding that rats with lesions of this area show deficits in spatial processing. While at least one study attempting to relate the functioning of this area to that of primates found that rats with PPC lesions show unilateral neglect (King & Corwin, 1993), several studies have failed to show the deficits of utilization of close personal space as found in primates (Rosner & Mittleman, 1996; Ward & Brown, 1997). Rather, the majority of spatial deficits uncovered in rats with PPC lesions are best described as affecting more distant extrapersonal space, a region less important for sensory-motor transformation than for navigational behavior. Rats with lesions of PPC are impaired at processing a change in the topological arrangement of cues in the environment (DeCoteau & Kesner, 1998; Goodrich-Hunsaker, Hunsaker, & Kesner, 2005; Save, Poucet, Foreman, & Buhot, 1992; Tees, 1999) and in locating a food reward relative to landmarks (Kesner, Farnsworth, & DiMattia, 1989). Given this apparent deficit at utilizing allocentric features of the environment, it is not surprising that these animals show poor performance in landmark navigation tasks such as the Morris water maze (DiMattia & Kesner, 1988; Kolb & Walkey, 1987). In addition to showing deficits of landmark navigation, there is increasing evidence that rats with PPC lesions are impaired at navigation by path integration (Commings, Gemmell, Anderson, Gigg, & O'Mara, 1999; Parron & Save, 2004; Save et al., 2001; Save & Moghaddam, 1996). For instance, Save et al. (2001) assessed the path integration abilities of rats with hippocampal and PPC lesions using the food-carrying task initially described by Wishaw and Tomie (1997). In this task, the animal is allowed to emerge from its nest box underneath a large circular table, search the table for a hidden morsel of food, and carry the food back to the nest for consumption. Despite taking a meandering path during the outward foraging phase, normal animals are able to return relatively directly to the nest even in the absence of visual landmarks (Wishaw & Hans Maaswinkel, 1998). Save et al. (2001) found that animals with PPC lesions were impaired at returning directly to their nest, providing evidence that these animals suffered from path integration deficits. Finally, while most of the above studies can be considered to test allocentric spatial processing, animals with PPC lesions have also been shown to possess deficits in tasks emphasizing egocentric processing. Rogers and Kesner (2006) trained rats with hippocampal or parietal lesions on two versions of a Hebb-Williams maze. In the allocentric version, the walls of the maze were translucent and the animals could use various landmarks outside the apparatus to guide behavior. In the egocentric version, the walls were opaque, depriving the use of visual landmarks and, hence, the animals were thought to have used an egocentric strategy. Using this approach, the authors found a double dissociation during acquisition, with the hippocampal lesioned animals showing the greatest impairment in the allocentric task and the parietal lesioned animals being most impaired in the egocentric version of the task. Interestingly, when a retention test was utilized in a follow-up study by training the animals on the task before administering the lesions, the parietal lesions affected both allocentric and egocentric retention while the hippocampal lesions had a much more limited affect on each task. These findings suggest that the PPC is important in the manipulation of previously acquired spatial

representations, regardless of whether an allocentric or egocentric frame of reference is being utilized.

Further evidence of the role of this brain region in navigation comes from electrophysiological studies that have found cells in PPC that respond to navigationally important task features. These recordings have typically been conducted while the animal is freely moving and performing on a maze or similar task. Using this approach, McNaughton and colleagues found a large number of cells in the PPC region that showed preferential activity for specific behavioral responses on a radial arm maze (McNaughton, Mizumori, Barnes, Marquis, & Green, 1994). Some cells became active during movement towards or away from the center, others during turns to the left or right, and still other cells became active when the animal was motionless. Using a more elaborate maze task, Nitz (2006) found that activity of most PPC cells could not be explained by a single variable such as direction of motion, location, or movement distance. Rather, activity was most tightly coupled to the progression of the animal along the route being traveled. As an example, a cell that fired at the outset of a journey before the first turn would also fire at the outset of the return trip, distinguishing this activity from simply being direction or place specific. Nitz suggested that these PPC cells encoded the order of both individual and multiple navigational epochs in a route and served as one of the neural substrates underlying navigation. In contrast to these previous studies, Nakamura (1999) recorded from rat PPC using a task similar to those typically used for monkey recordings. Specifically, the head of the animal was immobilized and the animal was required to remember the spatial location of stimuli (auditory tones in this case) in a delayed-nonmatching-to-sample task. In this paradigm, nearly half of PPC neurons were spatially tuned, i.e., they responded preferentially to a tone presented at a particular location relative to the animal. Furthermore, most of these cells exhibited a “memory” response, where they maintained an elevated rate of activity during the delay between the sample and matching tones. Interestingly, when the rat was rotated so that it was facing a different direction, the most consistent finding was that the cells maintained the same directional preference relative to the world, suggesting that the spatial position of the stimuli were encoded using an allocentric frame of reference. While this finding of allocentric spatial signals in the rat PPC is in contrast to the typically egocentric responses seen in primate PPC (Buneo & Andersen, 2006; Colby & Goldberg, 1999; Medendorp, 2008), it would suggest a specific role in the rat PPC for processing allocentric landmarks.

Finally, the rich pattern of connections of PPC with neocortical sensory and motor areas along with limbic areas linked to spatial processing provides further evidence that PPC may play an important role in navigational behavior. Figure 1 presents a diagram of these connections. PPC shares cortical connections with primary and secondary visual cortex (Kolb & Walkey, 1987; Miller & Vogt, 1984; Reep, Chandler, King, & Corwin, 1994), auditory cortex (Reep et al., 1994), somatosensory cortex (Kolb & Walkey, 1987; Reep et al., 1994), frontal association cortex (Kolb & Walkey, 1987; Reep et al., 1994; Reep, Corwin, Hashimoto, & Watson, 1987), and retrosplenial cortex (Kolb & Walkey, 1987; Reep et al., 1994). While the connections with neocortical sensory and motor areas provide for the possibility of navigationally important stimuli reaching PPC, the connection between PPC and the retrosplenial cortex could act as a conduit for information transfer between cortical and subcortical structures, many of which contain cellular correlates of allocentric space. Retrosplenial cortex projects to postsubiculum (Vogt & Miller, 1983), an area where head direction (HD) cells were first found (Ranck, 1984; Taube, Muller, & Ranck, 1990). HD cells fire based on the allocentric direction the animal is facing and are commonly thought to form the basis of the “sense of direction” of the animal (Taube, 2007). Retrosplenial cortex also projects to the entorhinal cortex (Wyss & Van Groen, 1992), the dorsal-medial portion of which contains grid cells. Grid cells fire in a repeated gridlike pattern based on the position of the animal in an environment (Hafting, Fyhn, Moden, Moser, & Moser, 2005), and have been conceptualized as being an important cellular constituent of the path integrator module (Fuhs & Touretzky, 2006; McNaughton, Battaglia,

Jensen, Moser, & Moser, 2006). The entorhinal cortex is the primary cortical input to the hippocampal complex where place cells, cells that encode the location of an animal in a known environment, were initially discovered by O'Keefe and Dostrovsky (1971). Finally, retrosplenial cortex is also connected to lateral dorsal and anterior dorsal thalamic nuclei (Sripanidkulchai & Wyss, 1986; Van Groen & Wyss, 1992, 1995) both of which contain HD cells (Mizumori & Williams, 1993; Taube, 1995). To summarize, the extensive connections of PPC with sensory and motor cortex as well as cortical and subcortical limbic areas linked to spatial processing provides the opportunity for PPC to play an integral role in exchanging higher order cortical signals used for navigation with limbic structures containing cell types showing various spatial correlates.

Role of PPC in Cellular Correlates of Navigation

In light of the previously described behavioral, electrophysiological, and anatomical data suggesting that PPC may be an important structure for navigation, and the connectivity of this area with areas containing place, HD, and grid cells that seem to provide signals reflecting navigational behavior, it would be interesting to determine how the activity of these cellular correlates change as a result of PPC lesions. Utilizing this approach, Save, Paz-Villagran, Alexinsky & Poucet (2005) recorded from CA1 hippocampal place cells in animals that had received bilateral lesions of PPC. Besides assessing the stability and basic spatial characteristics of recorded place cells following PPC lesions, the authors rotated and removed the landmarks within the recording cylinder to determine if the lesions affected landmark control of place fields. While cells from lesioned animals were relatively normal in many respects, they appeared to be less controlled by the landmarks in the apparatus, with nearly a quarter of cells showing place fields that failed to shift with the landmarks as in normal animals. Even more dramatic, when the rotated landmarks were removed from the apparatus in view of the animal, nearly all the place fields from lesioned animals returned to their pre-rotated positions. This shift was in contrast to cells from normal animals, which remained in phase with the position of the removed landmarks. In explaining these results, the authors concluded that animals with PPC lesions show an impaired ability to orient to proximal* landmarks and so when those landmarks within the enclosure were removed, the remaining distal landmarks were used for orientation. This finding and subsequent interpretation is consistent with a previous finding by Save and Poucet (2000b) demonstrating that animals with PPC lesions show selective deficits in the utilization of proximal landmarks. It is possible that the inability to process proximal cues is due to a spatial deficit in understanding the topological relationships amongst different items, as reported by Goodrich-Hunsaker and colleagues (2005) in parietal lesioned animals.

Landmark and Idiothetic Control of HD cells in Animals without a PPC

To explore the interaction between PPC and the HD system, we recently recorded the activity of anterior thalamic HD cells in rats that had received bilateral PPC lesions (Calton, Turner, Cyrenne, Lee, & Taube, 2008). Although there are no direct connections between anterior thalamic HD cells and the PPC, anterior thalamic HD cells are reciprocally connected with the postsubiculum, which, as described above, receives PPC input via the retrosplenial cortex. Because HD cells are more numerous in the anterior thalamus than in the postsubiculum, this area was a good place to start with in terms of examining the influence of the PPC over the HD cell system. Because of disagreement in the lesion literature regarding the location of PPC (see above), we utilized two lesion sizes. Some animals received large lesions with anterior-posterior coordinates spanning +0.5 mm to -6.0 mm relative to bregma, which were intended

*Proximal cues are those potential landmarks that are nearby or contained within the behavioral enclosure. In contrast, distal cues are potential landmarks that are further away from the animal, often outside the enclosure.

to include nearly all the previous lesion sites ascribed to PPC. Other animals received smaller lesions with AP coordinates spanning -2.0 mm to -6.0 mm relative to Bregma and these lesions were intended to include the more posterior site that has been used most commonly (e.g., Kolb & Walkey, 1987; Save & Poucet, 2000b). Interestingly, there was essentially no difference in findings between the two lesion sizes and so the results of these conditions will be combined in this summary.

Figure 2A presents the basic procedure of the study. The cylinder task assessed the effects of PPC lesions on the basic firing characteristics of anterior thalamic HD cells and whether PPC is necessary for accurate landmark control of the directional signal carried by the HD network. Cells from control and PPC lesioned animals were recorded while the animal foraged in a cylindrical enclosure, and the salient visual landmark in the enclosure (a white card attached to the wall) was moved between sessions to determine landmark control of HD cell activity. To reduce the influence of landmarks other than the white card, a curtain surrounded the entire apparatus, a white noise generator was utilized to mask potential auditory cues, and the floor paper was changed between sessions to eliminate olfactory cues. In this task, we found no difference between control and lesioned animals in the basic directional characteristics of recorded HD cells such as directional information content, directional firing range, signal-to-noise ratio, and peak firing rate (Fig. 2B). The finding that PPC lesions did not alter the basic firing characteristics of anterior thalamic HD cells was not surprising, as a number of investigations have indicated that the driving input into the HD system originates in the vestibular organs and involves the reciprocal connections between the dorsal tegmental and lateral mammillary nuclei with minimal cortical influence before reaching anterior thalamus, the site of our recordings (Fig. 1; reviewed by Sharp, Blair, & Cho, 2001; Taube, 2007). What was surprising was that, given the detrimental effects of PPC lesions on landmark guided navigation (Dimattia & Kesner, 1988; Kolb & Walkey, 1987; Save & Poucet, 2000b) and on landmark control of place cell stability (Save et al., 2005), we found no difference between control and PPC lesioned animals in the visual landmark control of HD cells. In both control and PPC lesioned animals, the preferred directions of recorded cells shifted in concert with the position of the landmark in the apparatus (Fig. 3A-B). In addition, this intact landmark control of anterior thalamic HD cells in PPC-lesioned animals provides an additional insight into the role of this cortical area in the operation of the HD cell system. McNaughton, Chen, and Markus (1991) have suggested that in order for a landmark to gain the ability to influence the navigational circuitry, it must become associated with a preexisting stable directional reference. In a similar way, Save and Poucet (2000a) suggested that PPC contributes to the binding of landmark and self-motion cues into an enduring spatial representation, suggesting that an intact PPC might be necessary for a landmark to become a stable allocentric reference. In our study, animals were not exposed to the recording apparatus and the visual landmark until after surgical recovery, providing evidence that the PPC was not necessary for the development of the ability of a visual cue to exert control over the HD signal.

While the cylinder task provided an assessment of the role of PPC in the landmark control of the HD network, we also utilized a dual-chamber task to determine the role of PPC in the use of idiothetic cues by the HD system (Figure 2A). In this task, first described by Taube and Burton (1995), the animal initially forages inside a cylindrical enclosure similar to that used in the cylinder task. After assessing anterior thalamic HD activity in this enclosure, a hidden door is opened that allows the animal to walk through an unfamiliar passageway composed of two right angle turns, which eventually ends in a novel rectangular enclosure. The animal is then locked in this novel enclosure to assess HD activity. Because the visual landmarks of the cylindrical enclosure are absent in the passageway and rectangular enclosure, the ability of the HD system to maintain a consistent preferred direction between the enclosures is likely dependent on the use of self-motion cues. In short, the navigational system must perform a path integration in order to maintain an accurate directional reference between the cylindrical

and rectangular enclosures. Figures 4A and 4B present sample tuning curves and scatter diagrams of the shifts between preferred directions in the cylindrical and rectangular enclosures in control animals and animals with PPC lesions (Calton et al., 2008). An examination of these angular deviation values suggests a slight difference in stability between control animals and animals with PPC lesions, but not the dramatic difference one would expect if PPC is necessary for the use of idiothetic signals by the HD system. Statistical analysis bears out the equivocality of the data -- while the absolute angular shifts were significantly larger in animals with PPC lesions, these scores were still significantly tuned around a central point and the concentration of the scores was not significantly different between the control and lesioned groups (Batschelet, 1981).

One possible explanation of the relatively stable directional signal between the two enclosures in lesioned animals is that the dual-chamber task is too simple and does not adequately test the path integration ability of the HD network. However, as Figure 4C shows, previous studies from our laboratory demonstrated that this task was sensitive to other manipulations. Specifically, Golob and Taube (1999) showed much less directional stability of anterior thalamic HD cells in this task in animals with hippocampal lesions, and Stackman, Golob, Bassett, and Taube (2003) similarly showed unstable preferred firing directions in normal animals that were moved between the enclosures in a cart thereby depriving the HD network of the normal proprioceptive and motor efference copy cues that usually accompany self-locomotion. In short, given the modest impairments in animals with PPC lesions relative to other manipulations, we interpret the dual-chamber results to indicate that PPC is not necessary for the HD system to utilize idiothetic cues for the maintenance of a stable directional signal.

Given our findings that the PPC is not necessary to carry landmark and idiothetic signals into the HD system, we can postulate where these signals may be originating. As mentioned above, the HD signal is believed to be generated amongst the reciprocal connections between the dorsal tegmental and lateral mammillary nuclei, as lesions of either area disrupt direction-specific firing downstream in the anterior thalamus (Bassett, Tullman, & Taube, 2007; Blair, Cho, & Sharp, 1998). Further, landmark control of HD cell responses in the anterior thalamus and lateral mammillary nuclei are disrupted by lesions of the postsubiculum, despite an intact PPC (Goodridge & Taube, 1997; Yoder & Taube, 2008); and lesions of either the hippocampus or entorhinal cortex do not disrupt landmark control of anterior thalamic HD cells (Clark & Taube, 2008; Golob & Taube, 1997). Because visual cortex projects directly to the postsubiculum in the rat (Vogt & Miller, 1983), it is likely that these projections carry the necessary landmark information to the HD cell circuit. Self-motion information, both vestibular and motor/proprioceptive, is most likely processed subcortically for HD cells (see Taube, 2007 for a discussion of this issue), possibly through ring attractor network mechanisms (Skaggs, Knierim, Kudrimoti, & McNaughton, 1995; Zhang, 1996).

Proposed Role of PPC in Navigational Behavior

Our findings of intact landmark and path integration signals within the HD network following PPC lesions stand in contrast to the spatial deficits observed in behavioral studies following PPC lesions and the electrophysiological studies discussed above indicating a role of PPC in navigation. How can these disparate findings be reconciled? First, it is important to note that the existence of stable directional representations in the place and HD cell networks following PPC lesions do not necessarily negate the role of PPC in navigational behavior. Several studies have demonstrated that the behavior of an animal does not always reflect the directional signal found in the HD or place cell network. For instance, Golob and colleagues recorded HD cells while the animals performed a directional reference-memory task (Golob, Stackman, Wong, & Taube, 2001). In this task, water deprived animals were reinforced for approaching a particular corner of a square enclosure based on the location of a cue attached to one wall of

the enclosure. Not surprisingly, because task performance was high, and HD cells typically show stable preferred directions during recording sessions, there was generally a consistent relationship between the correct corner choice of the animal and the preferred direction of the recorded cell. However, in almost a quarter of the trials the preferred direction of the cell shifted spontaneously when the animal was placed in the apparatus at the start of a trial. Because this instability is not seen in cylindrical enclosures and these shifts were usually in multiples of 90°, they were hypothesized to have occurred as a result of the square enclosure providing additional geometric orienting cues. In those instances when the preferred direction of the cell shifted, the animals still chose the correct corner 73% of the time, only slightly less than the 78% correct choice rate when the cell was stable. This finding is strong evidence that whatever signal was used to guide corner selection, the choice was not simply a function of the HD signal. A similar disconnect between place cell activity and behavior was reported by Jeffery, Gilbert, Burton, & Studwick (2003), where rats continued to accurately choose a rewarded corner despite a contextual change that led to place cell remapping. Studies such as these suggest that while one or more representations of allocentric space likely exist in the navigational circuitry of HD cells, place cells, and grid cells, the integration of these spatial constructs into a cohesive map of the world and the final decision of how or when to utilize these representations to guide behavior is made elsewhere. Given the previously described literature linking PPC to spatial behavior, it seems reasonable that PPC may serve the role of integrating these various spatial representations into a coherent framework. The decision of how this information will be used is possibly made by prefrontal areas.

Consider the scenario in which an animal must accurately return home after a long foraging excursion. At any stage of this journey the sense of current location and sense of direction of the animal are processed by the place and HD cell systems, mostly independent of each other, as lesioning one system does not greatly affect the basic spatial signals carried by the other (Calton, Stackman, Goodridge, Archey, Dudchenko, & Taube, 2003; Golob & Taube, 1997). To be of use during navigation, these two types of information must be integrated to represent the animal's current spatial orientation (location and directional heading relative to allocentric references). In addition to maintaining a sense of spatial orientation, at various choice points along the journey the animal must determine the most appropriate route to take. This will require integration of the animal's spatial orientation with information about the location of the goal and a computation performed to formulate the most direct route to the goal. Whether the process of determining a route is part of the same process as manipulating the different spatial relationships, or is a distinct and separate process remains to be elucidated. Finally, the plan must be executed. From this view, it is easy to see how navigational impairments can come about for a number of reasons – namely, a problem with perceiving one's orientation, a problem in representing one's orientation with an intended goal, a problem in performing the necessary computation to move in the direction of the final goal, or a problem in executing the navigational plan. We therefore postulate that parietal damage does *not* interfere with the perception of one's spatial orientation or in the actual execution of the planned route, but rather with the integration of spatial information about oneself and the intended goal, along with the operation required to compute a trajectory between oneself and the goal. Thus, it is the manipulation of the different types of spatial information and the subsequent computational aspects of charting a route to a goal that the PPC is essential for. The other functions, perceived spatial orientation and execution of planned route, are likely processed in limbic system circuitry and prefrontal areas, respectively.

The integration of various types of spatial information by the parietal cortex may explain some of the behavioral and spatial deficits often observed following parietal lesions in rodents. For example, Kesner and colleagues have explored the role of the parietal cortex in various types of spatial tasks. Specifically, in a task that involved differentiating between the metric and topological relationships among two different objects, they found that hippocampal lesioned

animals were impaired on the metric version of the task and parietal lesioned animals were impaired on the topological version (Goodrich-Hunsaker et al., 2005). In another study, the authors reported that animals trained to perform the topological task first and then lesioned later were impaired following the parietal lesions (Goodrich-Hunsaker, Howard, Hunsaker, & Kesner, 2008). One common aspect of these two studies is that the animals had to understand the topological relationships among different items in order to perform the tasks accurately, an ability that likely involves manipulating the spatial representations amongst different items. Indeed, Cheng (1986) proposed that the brain contains individual modules that process the geometric content of the scene. Similarly, Poucet (1993) in his model of spatial cognition made a distinction between metric and topological representations. There are, of course, studies showing that animals with parietal lesions perform accurately on spatial tasks that at first glance appear to involve the types of spatial manipulations that we are attributing to the parietal cortex (e.g., Long & Kesner, 1996, 1998). However, it is likely that there is some redundancy in the spatial processing systems and that an intact hippocampus is sometimes capable of taking over the functions that are normally ascribed to the parietal cortex.

Parietal Cortex and the Cognitive Map

The integration of spatial representations involving the subject, various landmarks, and the intended goal has been referred to as the 'cognitive map,' and historically, the hippocampus was the postulated site of this map (O'Keefe & Nadel, 1978). However, it can be inferred from several studies that patients with hippocampal damage display little, if any, navigational impairments in already familiar environments despite being markedly impaired in novel environments. For example, the original study of H.M. by Scoville and Milner (1957) and subsequent studies on him by Corkin (1984) have documented profound anterograde amnesia, but neither of these studies have shown any major navigational impairments in familiar environments, despite the extensive battery of tests given to him. Corkin (1984, pg. 254) reports that "H.M. is able to draw an accurate floor plan of the house where he lived during the postoperative years from 1960-1974, showing all the rooms in their proper location. He believes that he still lives there and can recognize the floor plan, drawn by someone else, when it is presented with four foils. In the nursing home where he lives, he can find his way from the ground floor to his room, which is one flight up." Although it's possible that an actual navigational test in a familiar environment might uncover spatial deficits in H.M., other studies would suggest that this finding would not be the case. For example, Teng and Squire (1999) studied a patient (E.P.) with extensive bilateral hippocampal damage from encephalitis who had a profound impairment in recalling facts and events from the onset of his disease. Despite this severe amnesia he was able to recall places and their spatial layouts learned prior to his disease as well, or better than, age-matched controls. Further, Bohbot and Corkin (2007) recently reported that H.M. was generally able to locate a sensor underneath a carpet in a spatial task that was designed to be an analogue of the Morris water task. The authors attributed his accurate performance to an intact portion of his limbic area that included the parahippocampal cortex. However, it is possible that this functional ability was due to an intact parietal cortex – a possibility that was never ruled out. Finally, another recent study of patients with hippocampal lesions, some of whom also contained damage to the entorhinal cortex, revealed that they were as accurate as controls when pointing to and estimating the distance back to their start position after walking various paths – some of which were relatively short (~4 m) with 1-2 turns, while others were longer (15 m) and required on average 30 sec to perform (Shrager, Kirwan, & Squire, 2008). From this finding, the authors argued that path integration abilities were preserved in these patients (however, see Philbeck, Behrmann, Levy, Potolicchio, & Caputy, 2004).

Before leaving the discussion of spatial abilities in patients with medial temporal lobe damage, it is important to consider the spatial abilities of patients with Alzheimer's disease, since they

are notorious for getting lost (Cherrier, Mendez, & Perryman, 2001; De Leon, Potegal, & Gurland, 1984; Delpolyi, Rankin, Mucke, Miller, & Gorno-Tempini, 2007). Although, these patients show marked hippocampal pathology, Alzheimer's disease patients frequently display profound widespread damage to other non-hippocampal areas, including the parietal (Hof, Bouras, Constandinidis, & Morrison, 1989, 1990) and posterior cingulate cortices (Jones, Barnes, Uylings, Fox, Frost, Witter, & Scheltens, 2006; Minoshima, Giordani, Berent, Frey, Foster, & Kuhl, 1997; Nestor, Fryer, Ikeda, & Hodges, 2003; Scheff & Price, 2001), which makes it difficult to conclude that the hippocampus is the major contributor to the spatial deficits. Indeed, some Alzheimer's patients have been characterized as having Balint's syndrome (Hof et al., 1989, 1990; Mendez, Turner, Gilmore, Remier, & Tomsak, 1990), and lesions of the posterior cingulate cortex are well-known for leading to topographic disorientation and other spatial deficits (Giannakopoulos, Gold, Duc, Michel, Hof, & Bouras, 2000; Scheff & Price, 2001; Takahashi, Kawamura, Shiota, Kasahata, & Hirayama, 1997; Vogt, Finch, & Olson, 1992). Even for patients where the damage is confined to hippocampal systems, their spatial deficits might be attributed to the fact that they are in an unfamiliar environment and unable to encode new spatial relationships with their surroundings (Turriziani, Carlesimo, Perri, Tomaiuolo, & Caltagirone, 2003).

Taken together, these findings suggest that hippocampal-damaged subjects can maintain an accurate map-like representation of an environment and compute and execute a route to a goal. Our view is that a major portion of this function resides in the PPC, which is akin to saying that at least some aspect of the cognitive map is located here. In this way, one can consider the PPC to be a site for memory storage – in this case, memories that involve spatial relationships. This view would be consistent with the type of deficit often observed in humans and animals with parietal damage – namely topographical disorientation. In the human version of this disorder, patients can typically recognize landmarks, but have a poor understanding of their spatial configuration with one another (Brain, 1941; De Renzi, 1982; Hublet & Demeurisse, 1992; Ino, Usami, Tokumoto, Kimura, Ozawa, & Nakamura, 2008). The deficits are readily apparent when they are asked to draw sketch maps representing the spatial relationships of objects. Such deficits in understanding the spatial relationships amongst items would certainly lead to navigational impairments, particularly in the planning of a route.

At least in humans, the PPC is unlikely involved in the recognition of landmarks, as other functional imaging studies have shown that areas in the inferior temporal cortex, referred to as the parahippocampal place area (PPA), are important for this function (Epstein, Harris, Stanley, & Kanwisher, 1999; Epstein & Kanwisher, 1998). In contrast, both Aguirre and D'Esposito (1997) and Iaria and colleagues (2003) reported the activation of posterior parietal areas during tasks requiring knowledge about the spatial position and manipulation of objects or landmarks. Thus, the parietal cortex seems particularly important for representing and manipulating the spatial relationships amongst the different elements in the environment, whether they be extrapersonal objects, allocentric places, or the self. Consistent with this view is a recent study that revealed a dissociation between the perception of angular velocity versus the perception of angular displacement (Seemungal, Rizzo, Gresty, Rothwell, & Bronstein, 2008). Subjects were given repetitive transcranial magnetic stimulation (TMS) applied separately over either the left or right PPC while they performed an angular displacement task where they were passively rotated in a chair about the yaw axis in the dark. Then, after cessation of rotation and the TMS, they had to return themselves to the start position using a joy-stick. Prior to testing subjects were told to either use a displacement-matching strategy or a velocity-matching strategy to return the chair to its start position. The difference is that in the displacement matching strategy, the subjects had to imagine how much they were angularly displaced in space, whereas in the velocity-matching strategy subjects had to keep track of their angular speed and reproduce it to perform the task accurately. The authors found that TMS applied to either the right or left PPC disrupted performance when the subjects were required to use the

displacement-matching strategy, but not when they used a velocity-matching strategy. From these findings, the authors argued that perception of angular speed was derived from vestibular information, which in turn was projected rostrally through the thalamus as a velocity signal, and ultimately processed in the human analogue of the monkey parietal-insular vestibular cortex (PIVC)(Guldin & Grüsser, 1998). In contrast, the perception of angular displacement occurs in the PPC, where the vestibular-derived velocity signal undergoes a mathematical integration in time to yield angular displacement.

The results of most animal lesion studies on spatial navigation have been interpreted based on the animal's ability to utilize landmark or idiothetic cues, and/or whether the place or HD systems were left intact by the lesion. However, one important process necessary for accurate navigation that has been neglected is the ability to calculate and plan a route based on the animal's current spatial orientation and the intended goal. Given a known spatial orientation, it is essential that a subject perform some type of computation, whether mathematical or qualitative, of the path required to navigate to a goal. This calculation may take the form of predetermining a sequence of actions from the subject's starting position all the way to the goal, a process that can be called route planning. Alternatively, the subject may determine the general distance and direction required to attain the goal, and initiate movement in that direction – a trajectory, but does not have the entire route planned in detail. In this second scenario, the subject performs a series of computations and actions, where each computation and subsequent movement brings the subject closer to the goal, but there is an absence of an overall plan from beginning to end, at least at the start of the route. After some movement, the subject would have to update their orientation and compute a new trajectory from their current location. Note that these two operation types, route planning and trajectory movement, are not necessarily mutually exclusive. In any event, the location of the neural substrate for this operation is poorly understood.

Given the anatomical connections and the types of information present in the parietal cortex, the PPC seems like a good candidate for where this computational function may be accomplished, and would go hand-in-hand with the ability to manipulate different spatial representations. This view would be consistent with the findings by Nitz (2006) showing that cells in the PPC displayed activity based on a particular path traversed by the animal in a maze that contained several possible routes to a goal. It would also be consistent with recent parietal recordings from a monkey performing a navigation task in a virtual environment, where the majority of neurons displayed movement-selective activity at specific locations (Sato, Sakata, Tanaka, & Taira, 2006). Moreover, some of the lesion studies discussed above can be reinterpreted based on this view. For example, as discussed above Save et al. (2001) found that parietal-lesioned animals performed poorly in a spatial task requiring path integration, and argued that the parietal cortex was important for path integration. However, it is also possible that the animals were able to use path integration to maintain an accurate perception of their orientation, but could not integrate the spatial information about their perceived orientation with that of the goal location and were therefore unable to ‘chart’ an accurate route. Further, our view would also be consistent with the electrophysiological studies of place and HD cells showing that there were relatively intact representations of perceived location (Save et al., 2005) and directional heading (Calton et al., 2008) following parietal lesions, because in our view these functions are performed in non-parietal areas within the limbic system.

This view of PPC functioning in spatial operations is compatible with both egocentric and allocentric perspectives and thereby serves to integrate the sometimes disconnected views of this brain area between the primate and rodent literature. As mentioned earlier, the human and monkey literature primarily implicates the PPC in egocentric operations, such as the planning of limb movements to targets close to the body, while the rodent literature has more commonly emphasized the role of this brain area in allocentric navigation. We believe this difference to

be mostly due to the methodologies and behavioral tasks employed, rather than an intrinsic difference in the functioning of the PPC between higher and lower animals. Egocentric and allocentric representations have been simultaneously found in both primates (Snyder et al., 1998) and rodents (McNaughton et al., 1994), and on the basis of lesion and recording data it is reasonable to assume that there are dedicated regions or circuits within PPC devoted to each type of operation. While we have mostly concerned this review with allocentric processes, our postulated role of PPC may be similarly extended to egocentric operations, and in many respects is consistent with the current egocentric view of PPC as enabling the transformation of a spatial signal to the appropriate motor coordinates that enable an accurate limb or eye movement.

Conclusions

In summary, we view a major role of PPC to be that of integrating the perception of immediate space (i.e., spatial orientation) with more distant spatial representations in order to accurately formulate a route to the goal. In the context of allocentric navigation, subcortical and cortical limbic structures serve to construct a representation of location and directional heading using ascending and descending sensory signals, and this representation is sent to the PPC most likely via connections with retrosplenial cortex. PPC may then combine this spatial signal with other neocortically-generated signals (both spatial and non-spatial in origin) in determining an appropriate spatial plan to accomplish a goal-driven behavior.

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Figure 1.

Schematic diagram of connections between PPC, other cortical areas, and subcortical areas related to the HD circuit. Arrows represent direction of information flow between connected areas. Areas where grid, place, and HD cells have been found are indicated by the legend.

Figure 2.

A) Diagrams of the cylinder and dual-chamber task enclosures and procedures utilized by Calton et al. (2008). B) HD cells recorded from control and PPC lesioned animals were equivalent on the basic directional characteristics of directional information content, peak firing rate, signal to noise ratio, and directional firing range.

Figure 3.

HD cells from PPC lesioned animals showed normal visual landmark control in the Cylinder Task. *A*) Representative firing rate vs. HD tuning curves for HD cells from Control and PPC lesioned animals when the landmark was in the standard position (solid line), rotated 90° (dotted line), or returned to the standard position (dashed line). *B*) Scatter diagrams showing the amount of angular shift between cylinder task sessions for Control (top row) and PPC lesioned animals (bottom row). Each plot shows the angular shifts of preferred directions between pairs of sessions with the small circles representing the amount of angular shift of the preferred direction of single cells relative to the position of the cue card for the second session. The solid arrow denotes the expected mean vector angle if the angular shift is perfectly predicted by the cue card, and the dotted arrow denotes the observed mean vector angle. The length of the dotted arrow denotes the mean vector length, with a length of 1.0 (no variability in shift scores) represented by a vector spanning the radius of the circle. Each plot uses Cartesian coordinates with 0° at the 3 o'clock position and increasing values proceeding in a CCW direction.

Figure 4.

HD cells from PPC lesioned animals showed only a slight deficit in stability in the dual-chamber task. *A*) Representative Firing Rate/Head Direction tuning curves for HD cells from control and PPC lesioned animals while the animal was inside the cylindrical enclosure (solid line) and while the animal was inside the rectangular enclosure (dotted line). *B*) Scatter diagrams showing the amount of angular shift of preferred directions between cylindrical and rectangular enclosures of the dual-chamber task for control animals (upper panel) and PPC lesioned animals (lower panel). Black-filled circles represent cells from PPC lesioned animals, while gray-filled circles represent cells from PPC-Small animals. Arrows denote the mean vectors for each group. 0° is located at the 3 o'clock position with increasing degree values

proceeding in a CCW direction. C) Scatter diagrams of the directional shift of cells recorded in the dual-chamber task from animals with hippocampal lesions (Golob & Taube, 1999) and from animals that were moved between the two enclosures in a cart (Stackman, Golob, Bassett, & Taube, 2003).