Published in final edited form as:

Hippocampus. 2007 ; 17(8): 618–626. doi:10.1002/hipo.20298.

A navigational guidance system in the human brain

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Abstract

Finding your way in large-scale space requires knowing where you currently are and how to get to your goal destination. While much is understood about the neural basis of one's current position during navigation, surprisingly little is known about how the human brain guides navigation to goals. Computational accounts argue that specific brain regions support navigational guidance by coding the proximity and direction to the goal, but empirical evidence for such mechanisms is lacking. Here, we scanned subjects with functional MRI (fMRI) as they navigated to goal destinations in a highly accurate virtual simulation of a real city. Brain activity was then analysed in combination with metric measures of proximity and direction to goal destinations which were derived from each individual subject's coordinates at every second of navigation. We found that activity in the medial prefrontal cortex was positively correlated, and activity in a right subicular/entorhinal region was negatively correlated with goal proximity. By contrast, activity in bilateral posterior parietal cortex was correlated with egocentric direction to goals. Our results provide empirical evidence for a navigational guidance system in the human brain, and define more precisely the contribution of these three brain regions to human navigation. In addition, these findings may also have wider implications for how the brain monitors and integrates different types of information in the service of goal-directed behaviour in general.

Keywords

Navigation; goals; virtual reality; subiculum; medial prefrontal cortex; posterior parietal cortex

Introduction

The hippocampus is widely held to store or access the spatial representation of an environment and so facilitate navigation to unseen goals (O'Keefe and Nadel, 1978). Compelling evidence for this includes the spatially localised activity of hippocampal place cells which code for an individual's current position in the environment (Ekstrom et al., 2003; O'Keefe, 1976). Whilst knowledge of current position is clearly crucial, it is not sufficient for effective navigation in large-scale space. The primary purpose of navigation is to reach specific locations, or goals. Despite goals being the *raison d'être* of navigation, we know surprisingly little about how the brain represents goal locations or guides navigation to them.

While hippocampal place cells can show modulation of their spatially localised activity by future goals (Breese et al., 1989; Ferbinteanu and Shapiro, 2003; Frank et al., 2000; Hollup et al., 2001; Kobayashi et al., 1997; Lee et al., 2006; Wood et al., 2000) they do not appear to directly code for goal locations (Lenck-Santini et al., 2002; Speakman and O'Keefe,

1990). Several computational models have instead suggested that brain regions downstream from the hippocampus guide navigation by integrating the spatial information from many hippocampal place cells with additional goal-related information. Two variables in particular have been identified as important, namely the distance to the goal location or goal proximity, and the direction to the goal location (Bilkey and Clearwater, 2005; Burgess et al., 2000; Trullier and Meyer, 2000). In these models, goal proximity is coded by maximal activity of neurons at the currently sought goal location which then decreases as a function of the distance in every direction from the goal, independent of any barriers in the environment. Separate brain regions are thought to signal the egocentric direction to the goal by coding the angle between the current heading direction and the ideal direction to the goal (Burgess et al., 2000).

Despite having detailed predictions about the computational mechanisms guiding navigation, empirical evidence about which brain areas subserve goal location is lacking. It is thought that regions coding goal proximity might integrate spatial information from the hippocampus with reward-related information. Reward-related information has been highlighted because it might be useful for signalling the importance of goal locations. The subicular region (subiculum and presubiculum), nucleus accumbens, and medial prefrontal cortex (mPFC) have been suggested to code for goal proximity because they receive both spatial information from the hippocampus and reward-related information via dopaminergic inputs (Amaral and Witter, 1989; Gasbarri et al., 1994; Jay et al., 1989; Kelley and Domesick, 1982). While there is some evidence that the activity of cells in certain regions can be modulated by navigational goals (Ekstrom et al., 2003; Jung et al., 1998; Martin and Ono, 2000), only one study examining the rodent mPFC has found evidence of goal proximity coding (Hok et al., 2005). However, the activity was not selective for the goal being sought, as would be expected of a guidance signal. No evidence of cells coding the egocentric direction to goals has been reported, although the posterior parietal cortex has been implicated because of its known role in egocentric spatial processing (Andersen and Buneo, 2002; Burgess et al., 2000).

In summary, while precise predictions have been made about how the activity in a number of brain regions might code information about goals during navigation, no study has directly tested these predictions. Furthermore, very little is known at all about goal coding in the human brain during navigation. Here, we examined directly the neural bases of goal proximity and goal direction in humans during active navigation. We used the video game 'The Getaway' (© Sony Computer Entertainment Europe 2002) to present subjects with a highly accurate ground-level first person perspective of a simulation of central London, UK. Subjects' navigation in virtual London was recorded during fMRI, and their proximity and direction to goal destinations at every second along every route were calculated. These data were then combined with the fMRI time series, allowing us to establish the brain regions that maintained and updated goal signals during navigation.

Materials and Methods

Subjects

Twenty healthy right-handed male licensed London taxi drivers participated in the experiment (mean age 49.8 years, SD 8.5 years, range: 27 - 59 years). Taxi drivers were employed as subjects to ensure consistent and accurate navigation performance. The average time spent working as a licensed taxi driver was 18.3 years (SD 10.9 years, range: 1 - 38 years). All subjects had lived in London their entire lives or for the vast majority of it, and were naïve to the experimental stimuli. All subjects gave informed written consent to participation in accordance with the local research ethics committee.

The virtual environment

The video game 'The Getaway' (© Sony Computer Entertainment Europe 2002) run on a Sony Playstation2 (© Sony Computer Games Inc) was used to present subjects with a ground-level first person perspective view of a simulation of central London, UK (see Fig. 1, and Spiers and Maguire 2006a for a movie of navigation through the environment). In the game, over ~110km (~70 miles) of driveable roads have been accurately recreated from Ordnance Survey map data, covering approximately fifty square kilometres (~20 square miles) of the city centre. The game designers decided to truly recreate the city and a large team of photographers walked the streets of central London for two years recording details of the city. Buildings, shops, the one-way systems, working traffic lights, the busy London traffic, and an abundance of Londoners going about their business are all included. The 'Free Roaming' mode of the game was used, permitting free navigation with the normal game scenarios suspended. Subjects moved through the environment in a virtual London taxi cab controlled using a modified MRI-compatible game controller, consisting of two joysticks providing analogue control of acceleration, braking and steering left and right. To avoid constant collisions with other vehicles in the environment, Action Replay Max software (© Datel Design and Development Ltd 2003) provided a 'cheat' modification to the game, permitting subjects to drive through other vehicles if necessary. Subjects were instructed to drive 'legally' as they would in actual London. All of the taxi drivers confirmed that the game was very reminiscent of their experience of driving in central London.

Pre-scan training and familiarisation

Two weeks prior to scanning subjects were given two hours of practice with the game controls by asking them to navigate to various locations in areas of the environment not used in the experimental task. To avoid crashes with other vehicles and waiting for long periods at red traffic lights subjects were familiarised with being able to drive through cars and red traffic lights, but were otherwise required to comply with all other road traffic regulations in the UK. Thirty minutes before the scan subjects were again given further practice in an area not used in experimental tasks. During this practice session subjects were trained to respond to a set of recorded customers' requests to take them to goal destinations in London. Finally, inside the MRI scanner the subjects were given practice in an area of London not tested in the experimental tasks and with the MRI-compatible game control for between 2-3 minutes prior to the start of the experimental task. They were also given experience of hearing voices of customers over the noise of the scanner through head phones worn during the scan. Prior to scanning subjects were told the locations they would be starting from in the experimental tasks, but not the order.

Experimental tasks

During the fMRI scan subjects responded to customers' requests (heard via headphones) by delivering them to their required destinations within virtual London, whilst driving a London taxi. When the game came on the screen (view angle of 27.6 degrees), subjects were given between 3 - 5 seconds to orient themselves in the environment. Following this they heard a customer request a destination (mean duration 2.0 seconds). For all routes, at some point during navigation the subjects heard customers request a change of destination (mean duration 3.0 seconds). For three of the routes an additional request to avoid a location (1 route) or go via a location (2 routes) was made by the customer (mean duration 3.7 seconds). Seven routes were tested (3-6 minutes duration). Two subjects completed only four routes, in one case due to discomfort, the other due to a technical problem. Each block of navigation ended when either the subject reached the destination or when a predetermined period of time elapsed. Each block of navigation was separated by a period of rest in which the subjects viewed a blank white screen for 60 seconds. Total mean functional scanning time

was 31 minutes 35 seconds (SD 4 minutes 9 seconds). Subjects' navigation performance was recorded onto videotape for later analysis.

Calculation of goal proximity and egocentric direction to the goal

We focused our analysis on goal proximity (shortest linear distance) and egocentric direction to the goal because models of navigation specifically predict that populations of neurons in particular brain regions would code this information in their firing rate (Bilkey and Clearwater, 2005; Burgess et al., 2000; Trullier and Meyer, 2000). The brain may track other variables during navigation such as the path distance to the goal. However, unlike proximity and direction information, path distance does not provide a means of navigational guidance. People may not choose to take the most direct path to a goal destination, for example, in order avoid traffic congestion points or road works. Also, in a city like London, path distance is often affected by one-way systems, thus weakening its relationship with goal proximity. This is clearly evident in our task where there were instances on every route where subjects were in close proximity to the goal (e.g. location B on the route in Fig.2) but still had a long path ahead of them in order to reach the goal.

Proximity and direction data were derived as follows. Each subject's navigation performance was analysed in order to create a record of which street junctions were entered and when they were entered for each route. Information about where and when subjects stopped moving or made u-turns was also incorporated into this record. The latitude and longitude of each of the street junctions and stop/u-turn locations (totalling 582 locations) were determined using the program Google Earth (© Google 2005) and converted into Euclidean coordinates corresponding to Northings and Eastings on a transverse mercator projection using software from DMAP (© Alan Morton). Matlab (© Mathworks) was used to provide a linear interpolation over these coordinates to create an estimate of each subject's spatial position for every second of every route. A corresponding record of each subject's goal proximity and egocentric direction to the goal was then calculated from each of these coordinates and the coordinates of the goal locations (see Fig.2).

Goal proximity was calculated by finding the shortest linear distance between a subject's current location and the goal location and then re-scaling this between zero and one, where a value of one corresponded to being at the goal and a value of zero to being at the location furthest from the goal. Customers requested a change in goal destination at some point along each route. The goal coordinates changed to the new goal at that moment on each route. For two of the routes, the subject was also asked to go via a location. These 'via' locations were treated as goal locations.

To calculate the egocentric direction to the goal we first determined the current heading direction and the heading direction pointing to the goal at each location on each route. The current heading direction was determined by finding the phase angle between current location and the location of the subject one second later on the route. Because there was no future location for each final location, we assumed the subject was heading in the same direction at the final location as the location occupied one second previously. The heading direction pointing to the goal was determined by finding the phase angle between the current location and the goal location. To determine the egocentric direction to the goal, we first subtracted the current heading direction from the heading direction pointing to the goal. In this study, our main focus was on measuring overall variation in the egocentric direction towards the goal, thus we collapsed across left and right directions. This meant that values greater than 180 degrees were then subtracted from 360 degrees to bring all values into a range between 0 degrees (goal directly in front of the subject) and 180 degrees (goal directly behind the subject).

A measure of the total distance travelled for every second of every route was also calculated to examine the independence of goal proximity and egocentric direction from this additional changing variable. Distance travelled was calculated by initially determining the shortest distance between the current location and the location occupied one second previously. This was then added to the sum of the previously calculated distances travelled.

fMRI image acquisition and analysis

T2 weighted echo planar (EPI) images with BOLD (blood oxygen level dependent) contrast were acquired on a 1.5 tesla Siemens Sonata MRI scanner. We used standard scanning parameters to achieve whole brain coverage: 44 slices, 2mm thickness (1mm gap), TR 3.96 seconds, TE = 50 milliseconds. The first 4 volumes from each session were discarded to allow for T1 equilibration effects. A T1-weighted structural MRI scan was acquired for each subject. Images were analyzed in a standard manner using the statistical parametric mapping software SPM2 (www.fil.ion.ucl.ac.uk/SPM). Spatial preprocessing consisted of realignment, unwarping, normalization to a standard EPI template in MNI space with a resampled voxel size of 3×3×3mm and smoothing using a gaussian kernel with full width at half maximum of 10mm. Following preprocessing, statistical analysis was performed using the general linear model. A regressor consisting of events sampled once every second during the navigation periods was specified using a stick function and convolved with the haemodynamic response function. These events were parametrically modulated by two variables of interest: the goal proximity and the direction to the goal, to create regressors of interest. Rest periods were modelled with boxcar functions and auditory events (customer requests) and turning events were modelled with stick functions and all convolved with the haemodynamic response function to create the regressors of no interest. Second order parametric modulations (square of the goal proximity and cosine of the direction to the goal) were also modelled as regressors of no interest to account for non-linear effects. All parametric regressors were orthogonalised with respect to each other within SPM2 (Buchs et al., 1998). Subject-specific parameter estimates pertaining to each regressor (betas) were calculated for each voxel. The parameter estimates were entered into a second level random-effects analysis using t-tests.

We report results in apriori regions of interest at $p < 0.001$ uncorrected for multiple comparisons, with an extent threshold greater than seven contiguous voxels. Apriori regions of interest were based on predictions from models of navigation (Burgess et al., 2000) and previous neuroimaging studies of navigation (Hartley et al., 2003). These included the medial prefrontal cortex (Hartley et al., 2003; Yoshida and Ishii, 2006) the subicular region (including: subiculum, presubiculum and parasubiculum, see Duvernoy, 2002), nucleus accumbens, hippocampus (area covering CA1-CA3 and dentate gyrus) and posterior parietal cortex. Activations in other regions are reported if they survive correction for multiple comparisons across the whole brain at $p < 0.05$.

In order to verify the orthogonality of the current analysis from that previously reported (Spiers and Maguire, 2006a), we expanded the model described above by including regressors representing the conditions identified in the previous reported analysis. The same significant results of t-contrasts for goal proximity and egocentric direction to goals were found in this second model, thus confirming the orthogonality of the two research questions. In addition, we also created a model in which the distance travelled was included as a regressor, and another model in which the time periods when the goal was visible were removed from the goal proximity measure. Again similar results of t-contrasts for goal proximity and egocentric direction to goals were found, confirming that our current findings were independent from changes associated with the distance travelled in each route, and seeing the goal (for the latter model, $p < 0.005$ for mPFC).

In order to plot parameter estimates for different levels of goal proximity (see Fig.3) a new model was created in which goal proximity was modelled by eight regressors. Each regressor reflected $1/8^{\text{th}}$ of the total range of goal proximity in steps of 0.125 from 0 to 1. Thus, the first of these regressors reflected changes in goal proximity when the subject was far from the goal, while regressor eight reflected changes in goal proximity when the subject was close to the goal. The same procedure was applied to the egocentric direction to the goal (see Fig.4).

Results

Behavioural

As expected, all subjects completed the task successfully with 94% (SD 9%) of their routes being efficient. An efficient route was one where the subject moved continually closer to the goal given the constraints of London's one-way system and occasional obstructed streets that were included in the game. The mean speed travelled was 41.9 virtual km/hour (SD 7.6), and the mean total distance covered was 16.9 virtual km (SD 3.4).

fMRI

Aspects of the findings from this rich and flexible data set relating to different questions have been reported elsewhere (Spiers and Maguire, 2006a,b). We now report new analyses focused on the orthogonal issue of goal coding.

Goal proximity

Details of the brain areas where activity was significantly correlated with goal proximity can be found on Table 1 and Fig. 3 (see also Fig. 5). Activity in just two brain regions was correlated with goal proximity. A significant positive correlation was observed in the mPFC and a significant negative correlation was observed in a region extending from the right subiculum to the right entorhinal cortex. No significant positive or negative correlations were observed in the hippocampus or nucleus accumbens even at liberal thresholds ($p < 0.01$ uncorrected), or elsewhere in the brain ($p < 0.05$ corrected).

Egocentric direction to the goal

As with goal proximity, activity correlated positively with goal direction in very specific and focal brain regions, this time in bilateral posterior parietal cortex (see Table 1 and Fig. 4; see also Fig. 5). No negative correlations were observed. As before, no significant positive or negative correlations were observed in the hippocampus or nucleus accumbens even at liberal thresholds ($p < 0.01$ uncorrected), or elsewhere in the brain ($p < 0.05$ corrected).

Distance and time spent travelling to the goal

Because driving speed was relatively constant for all subjects, distance travelled to the goal and time to the goal both increased linearly within each route. No positive or negative correlations with distance travelled during a route / time spent travelling to the goal were observed in any brain region ($p < 0.05$ corrected).

Discussion

In this study we used fMRI and an accurate and interactive VR simulation of a complex real city to explore the brain regions in humans that support navigational guidance. We measured on a second-by-second basis the precise proximity and direction to specific goal destinations. This allowed us to test the prediction from computational models that during navigation, the relationship to goal locations is continuously tracked by brain regions whose

activity encodes either goal proximity (shortest linear distance) or egocentric direction to the goal. Our results revealed that activity in a select set of brain regions codes for goal destinations during navigation. Specifically, activity in the mPFC was positively correlated with goal proximity, while activity in the right subicular/entorhinal region was negatively correlated with goal proximity. By contrast, activity in bilateral posterior parietal cortex was significantly correlated with the egocentric direction to the goal. These results provide evidence for neural signals which could flexibly guide navigation over large distances to specific goals in familiar real world environments.

A medial prefrontal code for goal proximity

In contexts other than navigation, the prefrontal cortex is known to play an important role in processing future goals to guide actions (Genovesio et al., 2006; Miller and Cohen, 2001). The medial region in particular is thought to be involved in processing goal-related information when the relationship between our actions and our goals is liable to change (Matsumoto et al., 2003; Matsumoto and Tanaka, 2004). Our finding that mPFC activity correlates with goal proximity during navigation is consistent with this view, since coding goal proximity requires monitoring the spatial relationship between current location and the goal whilst negotiating obstacles in the environment. In addition, since reaching a goal is likely to be a rewarding experience, this result also accords with the suggestion that the mPFC is important for integrating information about future rewards (Knutson et al., 2005). Our results now show that in the context of goal processing the mPFC can integrate information from long-term memory about the Euclidean distances between locations in a familiar environment.

Several computational models have suggested that a neural code for goal proximity may be used to guide an animal to its goal (Bilkey and Clearwater, 2005; Burgess et al., 2000; Trullier and Meyer, 2000). Our results provide direct empirical support for this prediction and indicate that it is the mPFC which codes goal proximity, responding maximally near the goal. This finding is consistent with the suggestion that the mPFC is important for guiding navigation (Hok et al., 2005; Poucet et al., 2004). Lesions to the mPFC in rodents can impair navigation when behavioural flexibility is required (Lacroix et al., 2002) and cells in the mPFC have been found to code for goal locations during navigation tasks (Hok et al., 2005; Jung et al., 1998). In open environments these cells appear to have large place fields often peaked at goal locations (Hok et al., 2005). However, whether the cells could provide information aiding navigational guidance was not clear, as they responded whenever the animal was near a goal irrespective of whether that goal was the focus of current navigation or not. Modulation of activity by the current goal of navigation has been observed in cells of the frontal cortex in humans navigating in a VR environment (Ekstrom et al., 2003). However, no evidence of goal proximity coding was observed in the activity of those cells. Our results extend these previous studies by revealing that a neural representation exists in the mPFC which is both goal-selective and modulated by a spatial proximity code. In addition, our findings shed light on why activity in a similar region of mPFC region may have been observed to be active during previous neuroimaging studies of navigation (Gron et al., 2000; Hartley et al., 2003; Yoshida and Ishii, 2006). Our data suggest that the increased mPFC activity in navigation epochs may have derived in part from the processing of goal proximity.

A complementary goal proximity code in the right subicular/entorhinal region

A wide body of evidence indicates that the hippocampal formation is critical for spatial memory and navigation (Morris et al., 1982; O'Keefe and Nadel, 1978; Taube, 1998), but the contribution of different subregions to navigation is not well understood. Several computational models have proposed that goal proximity is coded by the subiculum or

presubiculum (Burgess et al., 2000; Trullier and Meyer, 2000). Our observation that activity in an area encompassing these regions is correlated with the goal proximity supports this proposal. The negative correlation with goal proximity indicates that activity in this region increases with the Euclidean distance from the goal. Such a signal could be used for navigational guidance based on gradient descent, where the navigator moves towards the location in the environment with the lowest firing rate.

The combination of two complementary goal proximity signals, one increasing (mPFC) the other decreasing (subicular / entorhinal region) with proximity, might provide a more efficient code than a single signal. This is because a single signal increasing with goal proximity would have a low firing rate whenever the animal is at large distances from the goal. Since low firing rates would be more susceptible to interference from background noise (Dayan and Abbott, 2001), such a signal would be poor at guiding navigation at large distances. Conversely, a signal decreasing with goal proximity would be poor at guiding navigation when the animal is near the goal. However, if navigation is guided by both signals it will be efficient across a whole range of distances.

An alternative explanation for why a negative correlation with goal proximity was observed might be that the subicular/entorhinal region could be sensitive to retrieval demands. In this view, retrieval demands are related to the size of the region to be navigated. Because this might decrease the nearer to the goal, retrieval demands might have a negative relationship with goal proximity. In our study the routes often contained segments where subjects were close to the goal but, because of London's one-way systems, still had to navigate through another substantial region of the city to reach the goal (e.g. location B on the route in Fig.2). This would mean that during these route segments both retrieval demands and goal proximity would be high, whilst during other segments one might be low while the other was high. Thus, we believe it unlikely that the subicular/entorhinal finding is due solely to retrieval demands. However, future studies are required aimed specifically at dissociating retrieval demands from goal proximity.

In the present study, the activated area covers both the entorhinal cortex and the subicular region, which may reflect the strong anatomical connections between these regions (Amaral and Witter, 1989) and similar electrophysiological responses (Sharp, 1999). Both regions have been found to signal location in a manner that is less environment-specific than the hippocampus proper (Frank et al., 2000; Sharp, 1997; Sharp, 1999; Sharp, 2006). Recently, medial entorhinal cells have been found to code a conjunction of distance, direction and speed in their firing rate, covering the environment with a grid-like pattern of firing peaks (Hafting et al., 2005; Sargolini et al., 2006). Such information may be important for spatial updating during navigation. Notwithstanding these exciting findings, how entorhinal and subicular representations are related to goal locations has received little attention. Subicular cells have been found to alter their activity during navigation to a goal (Martin and Ono, 2000), but it was not clear what was being encoded by such responses. Our data now suggest that goal proximity might be represented by cells in the subicular / entorhinal region.

The hippocampus and nucleus accumbens were not involved in coding goal proximity. The absence of a correlation with hippocampal activity is consistent with the predictions from computational models (Burgess et al., 2000; Trullier and Meyer, 2000), which suggest this function is served by other regions. The hippocampus and nucleus accumbens were found to be active specifically during periods of initial route planning in VR London (Spiers and Maguire, 2006a).

Egocentric direction to the goal is coded by posterior parietal cortex

Navigation also depends on determining the correct direction to travel to the goal. Cells in the rat presubiculum, anterior thalamus, and mammillary bodies known as head direction cells have been found to code current head direction relative to the cardinal axis of the environment (Taube, 1998). In the posterior parietal cortex, cells have been found that respond to the position of external stimuli relative to the retina, eye, head, trunk and world (Andersen and Buneo, 2002; Snyder et al., 1998). World-centred coding by neurons in area 7a in particular are thought to aid navigation (Snyder et al., 1998). Based on such evidence it has been suggested that the posterior parietal cortex translates directional information in cardinal coordinates (e.g. 20 degrees northeast) into an egocentric direction signal (e.g. 20 degrees left) necessary to guide movements to goal locations (Burgess et al., 2000). Our finding that activity in bilateral posterior parietal cortex codes the angular relationship between current facing direction and a heading direction pointing to the goal during navigation provides empirical support for this suggestion. Thus, regions within the posterior parietal cortex appear to aid navigation by coding information about the egocentric direction to the goal.

Conclusions

These results provide empirical evidence for a navigational guidance system in the human brain. Our findings support and refine computational models where signals of goal proximity and egocentric direction to the goal are posited to guide navigation. We show that activity in regions of the medial prefrontal cortex and right subicular/entorhinal area are directly linked to a spatial metric. Furthermore, we provide evidence that the posterior parietal cortex can code and monitor egocentric spatial information concerning distant locations beyond current sight during active navigation towards a goal. In summary, our findings reveal that an integrated system comprised of brain areas with complementary responses allows us to adapt to challenges in the environment in order to reach our goals.

Acknowledgments

This work was supported by a Wellcome Trust senior research fellowship in basic biomedical science to E.A.M. We are grateful to the pilot and scan participants for their time, patience, and good humour. We thank all the major licensed London taxi companies, publications, depots, and cafes for facilitating subject recruitment. We thank K. Friston, P. Dayan, D. Kumaran, B. de Martino, D. Hassabis for theoretical advice, K. Woollet for collecting the coordinates of locations in London, and P. Aston, E. Featherstone, C. Freemantle, R. Davis, O. Josephs, C. Hutton, J. Hocking, the FIL Methods Group, and the FIL Functional Technologies Team for their assistance.

Grant Sponsor: The Wellcome Trust, UK

References

- Amaral DG, Witter MP. The three-dimensional organization of the hippocampal formation: a review of anatomical data. *Neuroscience*. 1995; 31(3):571–91. [PubMed: 2687721]
- Andersen RA, Buneo CA. Intentional maps in posterior parietal cortex. *Annu Rev Neurosci*. 2002; 25:189–220. [PubMed: 12052908]
- Bilkey DK, Clearwater JM. The dynamic nature of spatial encoding in the hippocampus. *Behav Neurosci*. 2005; 119(6):1533–45. [PubMed: 16420157]
- Breese CR, Hampson RE, Deadwyler SA. Hippocampal place cells: stereotypy and plasticity. *J Neurosci*. 1989; 9(4):1097–111. [PubMed: 2703869]
- Buchel C, Holmes AP, Rees G, Friston KJ. Characterizing stimulus-response functions using nonlinear regressors in parametric fMRI experiments. *Neuroimage*. 1998; 8(2):140–8. [PubMed: 9740757]
- Burgess N, Jackson A, Hartley T, O'Keefe J. Predictions derived from modelling the hippocampal role in navigation. *Biol Cybern*. 2000; 83(3):301–12. [PubMed: 11007303]
- Dayan, P.; Abbott, LF. *Theoretical neuroscience*. Cambridge, Massachusetts: MIT Press; 2001.

- Duvernoy, HM. The human hippocampus. New York: Springer-Verlag; 2002.
- Ekstrom AD, Kahana MJ, Caplan JB, Fields TA, Isham EA, Newman EL, Fried I. Cellular networks underlying human spatial navigation. *Nature*. 2003; 425(6954):184–8. [PubMed: 12968182]
- Ferbinteanu J, Shapiro ML. Prospective and retrospective memory coding in the hippocampus. *Neuron*. 2003; 40(6):1227–39. [PubMed: 14687555]
- Frank LM, Brown EN, Wilson M. Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron*. 2000; 27(1):169–78. [PubMed: 10939340]
- Gasbarri A, Packard MG, Campana E, Pacitti C. Anterograde and retrograde tracing of projections from the ventral tegmental area to the hippocampal formation in the rat. *Brain Res Bull*. 1994; 33(4):445–52. [PubMed: 8124582]
- Genovesio A, Brasted PJ, Wise SP. Representation of future and previous spatial goals by separate neural populations in prefrontal cortex. *J Neurosci*. 2006; 26(27):7305–16. [PubMed: 16822988]
- Gron G, Wunderlich AP, Spitzer M, Tomczak R, Riepe MW. Brain activation during human navigation: gender-different neural networks as substrate of performance. *Nat Neurosci*. 2000; 3(4):404–8. [PubMed: 10725932]
- Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. Microstructure of a spatial map in the entorhinal cortex. *Nature*. 2005; 436(7052):801–6. [PubMed: 15965463]
- Hartley T, Maguire EA, Spiers HJ, Burgess N. The well-worn route and the path less traveled: distinct neural bases of route following and wayfinding in humans. *Neuron*. 2003; 37(5):877–88. [PubMed: 12628177]
- Hok V, Save E, Lenck-Santini PP, Poucet B. Coding for spatial goals in the prelimbic/infralimbic area of the rat frontal cortex. *Proc Natl Acad Sci U S A*. 2005; 102(12):4602–7. [PubMed: 15761059]
- Hollup SA, Molden S, Donnett JG, Moser MB, Moser EI. Accumulation of hippocampal place fields at the goal location in an annular watermaze task. *J Neurosci*. 2001; 21(5):1635–44. [PubMed: 11222654]
- Jay TM, Glowinski J, Thierry AM. Selectivity of the hippocampal projection to the prelimbic area of the prefrontal cortex in the rat. *Brain Res*. 1989; 505(2):337–40. [PubMed: 2598054]
- Jung MW, Qin Y, McNaughton BL, Barnes CA. Firing characteristics of deep layer neurons in prefrontal cortex in rats performing spatial working memory tasks. *Cereb Cortex*. 1998; 8(5):437–50. [PubMed: 9722087]
- Kelley AE, Domesick VB. The distribution of the projection from the hippocampal formation to the nucleus accumbens in the rat: an anterograde- and retrograde-horseradish peroxidase study. *Neuroscience*. 1982; 7(10):2321–35. [PubMed: 6817161]
- Knutson B, Taylor J, Kaufman M, Peterson R, Glover G. Distributed neural representation of expected value. *J Neurosci*. 2005; 25(19):4806–12. [PubMed: 15888656]
- Kobayashi T, Nishijo H, Fukuda M, Bures J, Ono T. Task-dependent representations in rat hippocampal place neurons. *J Neurophysiol*. 1997; 78(2):597–613. [PubMed: 9307098]
- Lacroix L, White I, Feldon J. Effect of excitotoxic lesions of rat medial prefrontal cortex on spatial memory. *Behav Brain Res*. 2002; 133(1):69–81. [PubMed: 12048175]
- Lee I, Griffin AL, Zilli EA, Eichenbaum H, Hasselmo ME. Gradual translocation of spatial correlates of neuronal firing in the hippocampus toward prospective reward locations. *Neuron*. 2006; 51(5):639–50. [PubMed: 16950161]
- Lenck-Santini PP, Muller RU, Save E, Poucet B. Relationships between place cell firing fields and navigational decisions by rats. *J Neurosci*. 2002; 22(20):9035–47. [PubMed: 12388610]
- Martin PD, Ono T. Effects of reward anticipation, reward presentation, and spatial parameters on the firing of single neurons recorded in the subiculum and nucleus accumbens of freely moving rats. *Behav Brain Res*. 2000; 116(1):23–38. [PubMed: 11090883]
- Matsumoto K, Suzuki W, Tanaka K. Neuronal correlates of goal-based motor selection in the prefrontal cortex. *Science*. 2003; 301(5630):229–32. [PubMed: 12855813]
- Matsumoto K, Tanaka K. The role of the medial prefrontal cortex in achieving goals. *Curr Opin Neurobiol*. 2004; 14(2):178–85. [PubMed: 15082322]
- Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001; 24:167–202. [PubMed: 11283309]

- Morris RG, Garrud P, Rawlins JN, O'Keefe J. Place navigation impaired in rats with hippocampal lesions. *Nature*. 1982; 297(5868):681–3. [PubMed: 7088155]
- O'Keefe J. Place units in the hippocampus of the freely moving rat. *Exp Neurol*. 1976; 51(1):78–109. [PubMed: 1261644]
- O'Keefe, J.; Nadel, L. *The hippocampus as a cognitive map*. Oxford: Oxford University Press; 1978.
- Poucet B, Lenck-Santini PP, Hok V, Save E, Banquet JP, Gaussier P, Muller RU. Spatial navigation and hippocampal place cell firing: the problem of goal encoding. *Rev Neurosci*. 2004; 15(2):89–107. [PubMed: 15202682]
- Sargolini F, Fyhn M, Hafting T, McNaughton BL, Witter MP, Moser MB, Moser EI. Conjunctive representation of position, direction, and velocity in entorhinal cortex. *Science*. 2006; 312(5774):758–62. [PubMed: 16675704]
- Sharp PE. Subicular cells generate similar spatial firing patterns in two geometrically and visually distinctive environments: comparison with hippocampal place cells. *Behav Brain Res*. 1997; 85(1):71–92. [PubMed: 9095343]
- Sharp PE. Complimentary roles for hippocampal versus subicular/entorhinal place cells in coding place, context, and events. *Hippocampus*. 1999; 9(4):432–43. [PubMed: 10495024]
- Sharp PE. Subicular place cells generate the same “map” for different environments: comparison with hippocampal cells. *Behav Brain Res*. 2006; 174(2):206–14. [PubMed: 16859764]
- Snyder LH, Grieve KL, Brotchie P, Andersen RA. Separate body- and world-referenced representations of visual space in parietal cortex. *Nature*. 1998; 394(6696):887–91. [PubMed: 9732870]
- Speakman A, O'Keefe J. Hippocampal complex spike cells do not change their place fields if the goal is moved within a cue controlled environment. *Eur J Neurosci*. 1990; 2(6):544–555. [PubMed: 12106024]
- Spiers HJ, Maguire EA. Thoughts, behaviour, and brain dynamics during navigation in the real world. *Neuroimage*. 2006a; 31(4):1826–1840. [PubMed: 16584892]
- Spiers HJ, Maguire EA. Spontaneous mentalizing during an interactive real world task: an fMRI study. *Neuropsychologia*. 2006b; 44(10):1674–82. [PubMed: 16687157]
- Taube JS. Head direction cells and the neurophysiological basis for a sense of direction. *Prog Neurobiol*. 1998; 55(3):225–56. [PubMed: 9643555]
- Trullier O, Meyer JA. Animat navigation using a cognitive graph. *Biol Cybern*. 2000; 83(3):271–85. [PubMed: 11007301]
- Wood ER, Dudchenko PA, Robitsek RJ, Eichenbaum H. Hippocampal neurons encode information about different types of memory episodes occurring in the same location. *Neuron*. 2000; 27(3):623–33. [PubMed: 11055443]
- Yoshida W, Ishii S. Resolution of uncertainty in prefrontal cortex. *Neuron*. 2006; 50(5):781–9. [PubMed: 16731515]

Figure 1.

The virtual environment of London (UK). Panels A and B show example views from within the video game 'The Getaway' © 2002 Sony Computer Entertainment Europe. Panel A shows a view at Piccadilly Circus, panel B shows a view at Trafalgar Square. These images are reproduced with the kind permission of Sony Computer Entertainment Europe. Panel C shows a map of the region of London that was used in the navigation task (not all the minor streets shown were included in the video game). Reproduced by permission of Geographers' A-Z Map Co. Ltd. © Crown Copyright 2005. All rights reserved. Licence number 100017302. Coloured lines indicate examples of typical routes driven by subjects to each of seven goal locations ('G') during the navigation blocks.

Figure 2.

Calculation of goal proximity and egocentric direction to goals. One example route from one subject is shown in order to illustrate how the goal-related data were derived. (A) The example route is the one shown in red in the centre of Fig.1C. It starts in Oxford Street, and has Peter Street as the goal location. The goal is marked with 'G' in the white semi-circle. Five locations are marked on the route (A-E), chosen to illustrate how the goal proximity and egocentric goal direction change along this route. Gray semi-circles represent the magnitude of the egocentric direction to the goal at each of these five locations. The values shown at the top and middle right of the route are the exact longitude and latitude of the grid lines they lie on. For the graphs in B and C, goal proximity and goal direction are plotted

against time, with the onsets of entry into the five locations (A-E) marked. (B) For the analysis, goal proximity values were re-scaled between one (at goal) and zero (at the maximum distance from the goal). (C) Egocentric distance was calculated by finding the angle between the current heading direction and the ideal direction to the goal. It was collapsed over left and right such that it was at a maximum when facing directly away from the goal (180 degrees) and zero when facing towards it (see Materials and Methods for details).

Figure 3.

fMRI results: goal proximity. Activations are shown on one subject's structural MRI scan with a threshold of $p < 0.001$ uncorrected (see Materials and Methods; see also Table 1 for details of peak coordinates, and Fig. 5 for parameter estimates). (A) A significant positive correlation was observed between goal proximity and activity in the mPFC, on the border between BA9 with 32a; left panel sagittal section, middle panel axial section. The right panel shows a plot of parameter estimates (arbitrary units) for eight different levels of goal proximity at the peak voxel in a representative subject (subject 1). (B) Left panel shows the significant negative correlation between goal proximity and activity in the right subicular/entorhinal region in coronal section. Other activated regions did not survive correction for whole brain volume. Three vertical panels in the middle show enlarged coronal sections in the medial temporal lobe at different anterior-posterior slices illustrating the distribution of the activation extending into the subicular region anteriorly and entorhinal region posteriorly. The right panel shows a plot of parameter estimates (arbitrary units) for eight different levels of goal proximity at the peak voxel in a representative subject (subject 13).

Figure 4. fMRI results: egocentric direction to goal. Activations are shown on one subject's structural MRI scan with a threshold of $p < 0.001$ uncorrected (see Materials and Methods; see also Table 1 for details of peak coordinate, and Fig. 5 for parameter estimates). (A) A significant positive correlation was observed between egocentric direction to goal and activity in bilateral posterior parietal cortex shown on an axial section. (B) A third more superiorly located activation was also observed in the right posterior parietal cortex, also shown on an axial section. (C) A plot of parameter estimates (arbitrary units) for eight different levels of egocentric distance to the goal at the peak voxel (shown in B) in a representative subject (subject 10).

Figure 5.

Summary of effects: parameter estimates. Parameter estimates (arbitrary units) from the peak voxels in the mPFC, right subicular/entorhinal region (R Sub/EC) and posterior parietal cortex (PPC). (A) Activity in mPFC increased while activity decreased in Sub/EC, with activity in parietal cortex relatively unchanged for goal proximity. (B) Activity in mPFC and Sub/EC was relatively unchanged, while parietal activity increased in relation to egocentric direction to the goal. Error bars are the 90% confidence intervals. See Table 1 for the peak coordinates and Z-scores.

Table 1

Peak coordinates for brain regions where activity correlated with goal proximity and egocentric direction to goal

Brain Regions	Z-score	Coordinates of peak activation		
		x	y	z
<u>Goal Proximity</u>				
Positive Correlation:				
Medial prefrontal cortex	3.98	3	30	39
Negative Correlation:				
Right subicular/entorhinal region	4.87	21	-18	-36
<u>Egocentric Direction to the Goal</u>				
Positive Correlation:				
Right posterior parietal cortex	3.70	24	-78	51
	3.47	27	-87	36
Left posterior parietal cortex	3.59	-18	-81	36
Negative Correlation:				
No regions active				

Activations statistically significant at $p < 0.001$ uncorrected. MNI coordinates are listed (see Materials and Methods, and Fig. 5 for parameter estimates).