

The Well-Worn Route and the Path Less Traveled: Distinct Neural Bases of Route Following and Wayfinding in Humans

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Summary

Finding one's way in a large-scale environment may engage different cognitive processes than following a familiar route. The neural bases of these processes were investigated using functional MRI (fMRI). Subjects found their way in one virtual-reality town and followed a well-learned route in another. In a control condition, subjects followed a visible trail. Within subjects, accurate wayfinding activated the right posterior hippocampus. Between-subjects correlations with performance showed that good navigators (i.e., accurate wayfinders) activated the anterior hippocampus during wayfinding and head of caudate during route following. These results coincide with neurophysiological evidence for distinct response (caudate) and place (hippocampal) representations supporting navigation. We argue that the type of representation used influences both performance and concomitant fMRI activation patterns.

Introduction

Navigation in a large-scale environment involves making decisions about which way to go based on one's current goals, internal representations, and perceptual cues. However, this behavior can be expressed in several different ways. We can choose a novel path when, for example, we have never previously traveled between two places or when the usual route is blocked. This implies a global form of representation or "cognitive map" of the environment in which landmark locations are represented in terms of their spatial relationships to one another (Tolman, 1948; O'Keefe and Nadel, 1978). Where such flexibility is not required, an alternative type of representation may be more useful. For example, when the same route is followed over and over again, a representation of the sequence of bodily movements may develop. While lacking flexibility, this type of representation might permit performance with less requirement for perceptual processing and conscious control, as seen in overlearned motor sequences (e.g., Jueptner et al., 1997a, 1997b).

In rats, both forms of representation can be seen in a popular spatial learning paradigm (Tolman et al., 1946; Tolman et al., 1947). The experiment uses a cross-shaped

maze where one arm has been sealed off to form a T shape. The animal starts at the base of the T, and each arm of the crossbar leads to a different goal box. Over many trials, the animal is trained to always go to the same goal box. On probe trials, the starting arm of the maze is switched to the opposite side of the junction, and the original starting arm is sealed. This manipulation places the direction of the body turn that the animals have been trained to perform in conflict with the physical location that they have been trained to visit. In this situation, some animals consistently turn in the same direction, implying the use of an action-based representation. Others consistently return to the previously baited location, implying the use of a cognitive map (i.e., a representation of the goal box in terms of its relationship to fixed landmarks in the laboratory). Interestingly, the two types of learning (called "response learning" and "place learning," respectively) have been shown to have distinct neural bases, with place learning depending on the hippocampus and response learning depending on the caudate nucleus. The resulting representations exist in parallel, but place learning takes place more rapidly than response learning, which results only from repeated training on the same fixed route (Morris et al., 1982; Potegal, 1972; Cook and Kesner, 1988; Kesner et al., 1993; Packard and McGaugh, 1996; O'Keefe and Nadel, 1978).

To date, functional neuroimaging studies of navigation in humans have not drawn a distinction between tasks that could be solved using an action-based representation (e.g., following a well-learned route) and those that require a novel route to be computed and thus imply the use of a cognitive map. Most used paradigms in which either form of representation might be applicable (e.g., Aguirre et al., 1996; Ghaem et al., 1997; Grön et al., 2000; Maguire et al., 1998a). In the current study, we designed "route following" and "wayfinding" tasks which, when performed accurately, would be expected to differentially engage the two types of representation and would thus expose any differences in their neural bases. Note that our distinction between route following and wayfinding does not relate directly to the distinction between "route" and "survey" representations investigated recently by Mellet et al. (2000) and Shelton and Gabrieli (2002). These studies focused on differences in the perspective used during learning: "route" knowledge being acquired from a ground-level perspective, and "survey" knowledge being based on an overhead perspective or map. In the current study, all experience of the environment was accrued at ground level.

Our principal aim was to explicitly compare the neural bases of wayfinding with those of route following, with the hypothesis that the hippocampus enables the former, while the caudate nucleus enables the latter. A related aim was to establish which brain regions contribute to the accuracy of navigation, as opposed to simply being engaged by the perceptual and motor requirements of attempting the task. A previous neuroimaging study examined navigational accuracy (Maguire et al., 1998a), identifying the hippocampus as critical to accu-

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rate navigation. However, due to the limitations of the positron emission tomography (PET) methodology used, it could not distinguish within- from between-subject variations in performance. The wide natural variation in navigational ability between subjects, coupled with recent findings of structural brain correlates of navigational experience (Maguire et al., 2000), indicate the importance of understanding individual differences in the neural bases of navigation. We hypothesized that the hippocampus would be more active in good navigators (compared to poor navigators) and in any individual when navigating well as opposed to poorly.

We constructed two virtual-reality (VR) environments in order to test these hypotheses. VR has several important advantages for this purpose; subjects are able to actively engage in first-person navigation and in environments that are naturalistic, despite being immobilized inside a scanner (with the unavoidable lack of direct somatosensory, motoric, and vestibular input this entails). In addition, the subject's behavior can be recorded at high spatial and temporal resolutions. As well as providing accurate measures of performance, this also allows us to model perceptual and motor aspects of the tasks on a fine timescale. Critically, this makes it possible to distinguish brain activity associated with these perceptual or motor variables from that associated with higher order cognitive processes. In order to avoid the confounding of place and response learning within the same environment, we used different VR environments for each of the learning types. Subjects learned about one town by free exploration. In the other, they repeatedly followed a fixed route. In the scanner, we tested their ability to find novel short routes in the first town (wayfinding) and to follow the familiar route in the second town (route following). The particular towns used and the order in which subjects were trained on the tasks were counterbalanced across subjects. For comparison, we also included a third task that did not require topographical memory, following a visible trail (trail following). Examples of stimuli from the experimental tasks are illustrated in Figure 1. See Experimental Procedures for further details.

Results

Behavioral Data

Subjects moved somewhat faster in the route-following condition (mean speed 3.45 ± 0.26 virtual ms^{-1}) than in trail following (3.34 ± 0.26 virtual ms^{-1}) and somewhat faster in trail following than in wayfinding (3.01 ± 0.36 virtual ms^{-1} ; $p < 0.05$ for all pair-wise comparisons). They also reached more of their targets in the route-following condition (48.69 ± 8.36 targets completed) than in trail following (32.69 ± 3.11) or wayfinding (26.00 ± 5.44 ; $p < 0.05$ for all pair-wise comparisons). The difference in the number of targets reached is partly due to the differences in speed, partly because navigation was more accurate for the well-learned route, and partly due to the relative proximity of consecutive landmarks in the route-following condition (where they were chosen so that no landmark was encountered while en route to another) compared with wayfinding and trail-following conditions (where this constraint did not apply).

Performance was measured by comparing the path taken during each task with the ideal path (see Experimental Procedures for details), with the distance error calculated as the additional distance traveled by the subject. Uncompleted trials (those targets that had not been reached by the end of each 50 s epoch) were excluded from the analyses. In the route-following condition, performance was close to ceiling, with very low distance errors in all subjects (between -2.0 and 9.8 virtual meters per epoch), indicating that they had all learned the prescribed route very well. Performance on the wayfinding condition was more variable, with individual average distance errors ranging between 7.0 and 32.2 virtual meters per epoch.

Trial-to-trial performance on the wayfinding task was incorporated into the model of the fMRI timeseries (below), so that regions specifically activated during accurate wayfinding could be distinguished from those activated during any attempt at the task.

Our model also explicitly included VR movement parameters (speed, rate and direction of turn) as covariates of no interest. Signal change strongly correlated with these parameters would effectively be removed from the task-related effects reported in the results section. For example, optic flow and some kinds of eye movement (e.g., optokinetic nystagmus) are strongly correlated with the subjects' virtual movement, and activation in corresponding visual (e.g., BA 17, 18, 19) and eye movement (e.g., the frontal eye fields) areas was associated with forward motion and turning, respectively, rather than with task-related variables.

fMRI Data

In the first instance, we report the direct comparisons between the main experimental conditions, revealing those areas activated by the attempt to perform each task. Note that because our model also incorporates a performance regressor, these direct task comparisons show activation independent of success on the task. Clearly, the regions of greatest interest are those specifically involved in successful performance. We therefore go on to report the main effect of trial-to-trial performance (within subjects) and correlational analyses of the relationship of activation to wayfinding performance between subjects. Except where otherwise indicated, all activations reported below exceed the $p < 0.001$ threshold for statistical significance (see Experimental Procedures for further details).

Performance-Independent Effects

The results of the direct comparisons between the tasks are shown in Figure 2. The areas activated in the wayfinding condition relative to the control condition of trail following include the posterior parietal, retrosplenial, fusiform and parahippocampal cortices, precuneus, caudate body, and cerebellum, as well as medial, ventrolateral, dorsolateral, and right anterior prefrontal cortices (Figure 2A). Comparison of the route-following condition with trail following showed notably less extensive cortical activation. Regions with significantly increased activity in the route-following condition included the caudate body, insula/ventrolateral prefrontal cortex, right anterior prefrontal cortex, and cerebellum (Figure 2B).

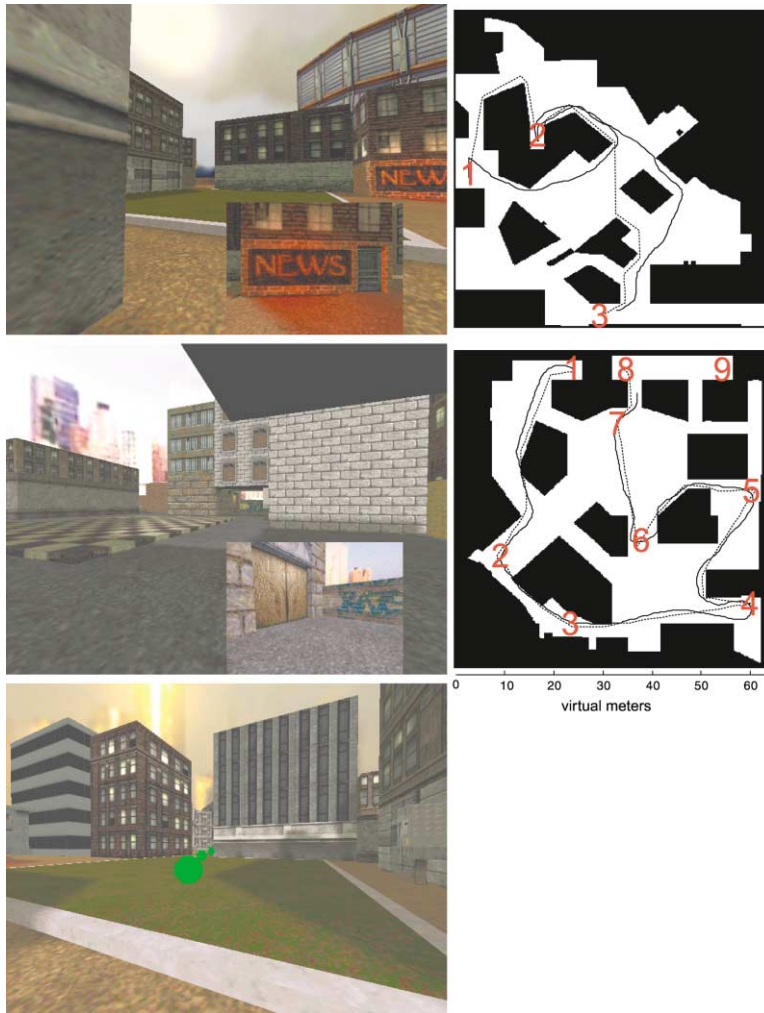


Figure 1. Example Views from the Virtual Town

(Top left) First-person display as seen by subjects in the scanner. Town 1 in the wayfinding condition. The current target is indicated in the bottom right part of the display.

(Top right) Map showing an example of the path followed by a subject (solid line) between the first three target locations (marked by numbers) at the beginning of an epoch. The corresponding ideal path is shown as a dotted line.

(Middle left) Town 2 in the route-following condition.

(Middle right) The map shows a subject's path during an entire 50 s route-following epoch. The successive target locations are marked by numbers.

(Bottom left) Town 1 during the trail-following condition.

The contrast of wayfinding and route-following conditions showed increased activation of the lateral posterior parietal cortex, cuneus, precuneus, retrosplenial cortex, and cerebellum for wayfinding (Figure 2C, red/yellow regions). In this contrast, there was also medial prefrontal activation and some involvement of ventrolateral and dorsolateral prefrontal cortices. The strongest cortical activations are seen in ventral occipital and medial temporal cortex (fusiform and parahippocampal gyri), with the strongest and most extensive activation on the right. The reverse contrast (Figure 2C, blue regions) shows increased activity in route following relative to wayfinding in the lateral parietal/somatosensory cortex, supplementary motor area (SMA), premotor and motor cortices, the insula/ventrolateral prefrontal and anterior superior temporal cortices.

Performance-Related Effects

The areas activated in attempting the wayfinding task (above) include many seen in previous studies of navigation, such as the parahippocampal, fusiform, retrosplenial, and parietal cortices. Given our hypotheses, there are some absentees from this pattern, most notably the hippocampus. The reasons for this become clear when we consider the areas specifically associated with accu-

rate performance of the task. These results are summarized in Table 1.

Within Subjects

What differentiates good navigation from poor navigation? For the within-subjects analysis, a measure of trial-by-trial accuracy was included in the general linear model (for the wayfinding condition only—performance on the route-following task was near ceiling for all subjects, see above). In two regions, activation varied reliably with accuracy, such that increased activation was associated with more accurate trials within subjects (Figure 3). They were the right insula (42, -12, 12) and right posterior hippocampus (30, -33, -3).

Between Subjects

What differentiates good navigators from poor navigators? The between-subjects analysis involved performing a correlation of a global measure of each individual subject's performance in the wayfinding condition with the degree of activation in the wayfinding condition relative to other conditions. A statistically significant positive correlation identifies regions more activated by good navigators than by poor ones.

First, regions showing activation in wayfinding relative to trail following that correlated with performance were examined; see Between Subjects W-T in Table 1. These

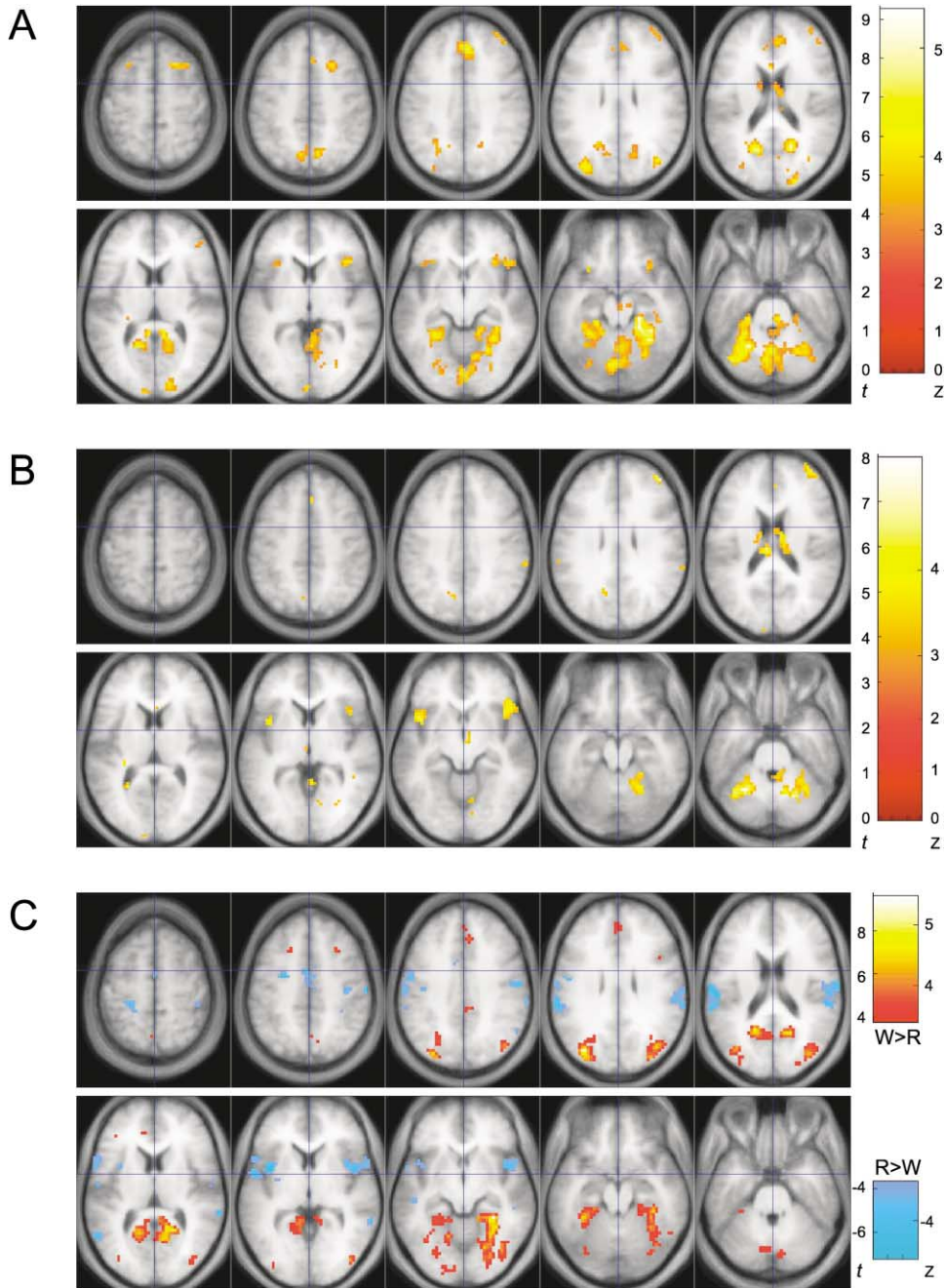


Figure 2. Summary of Activations from the Performance-Independent Task Comparisons

(A) Areas more active in the wayfinding than trail-following conditions. (B) Areas were more active in route following than trail following. (C) Red areas were more active in wayfinding than route following. Blue areas were more active in route following than wayfinding. Each panel (A–C) shows the mean normalized structural image of all subjects, sliced at 10 mm intervals from $z = 60$ to $z = -30$. For each contrast, $p < 0.001$, and regions smaller than 2 voxels are not shown. The cross hairs are at $x = 0$, $y = 0$ in each slice. Anatomical descriptions of the active regions are given in the text. The color bar indicates the t statistic associated with each voxel and Z score equivalent.

include a hippocampal activation whose location and extent are shown in Figure 4A together with a scattergram showing the correlation of performance and fMRI signal change for the peak voxel ($-30, -18, -15$; $r = 0.74$; $p < 0.001$). Note that this hippocampal activation is not strictly lateralized; we see the same trend in the right hippocampus, although the correlation does not reach significance ($30, -15, -18$; $r = 0.62$; $p =$

0.005). From examining the scattergram, it is also noteworthy that accurate navigators show increased hippocampal activity, while poorer navigators show decreased hippocampal activity. This may explain the absence of hippocampal activation in the performance independent comparisons, reported above.

Second, regions showing activation in wayfinding relative to route following that correlated with performance

Table 1. Performance Effects

[x, y, z]	Anatomical Location of Peak	Brodmann Area	Z Equivalent
Within-Subjects Wayfinding Performance			
[42, -12, 12]	R insula	BA 41/42	4.27
[30, -33, -3]	R hippocampus	—	3.29
Between-Subjects W-T			
[-9, 60, 30]	L superior frontal gyrus	BA 9	3.78
[-6, 39, 48]	L medial superior frontal gyrus	BA 8	3.35
[-54, -21, -15]	L superior temporal sulcus/middle temporal gyrus	BA 20/21	3.20
[-36, -9, -39]	L fusiform cortex	BA 20	3.91
[-30, -18, -15]	L hippocampus	—	3.36
[6, -66, 33]	R precuneus	BA 7	3.45
[-51, -48, 30]	L temporo-parietal junction	BA 40	3.41
[48, -45, 15]	R posterior superior temporal gyrus	BA 22	3.54
Between-Subjects W-Ro			
[-42, 21, 12]	L insula/inferior frontal gyrus	BA 44	3.75
[-51, 33, -9]	L inferior frontal gyrus	BA 47	3.18
[-18, 60, 18]	L superior/middle frontal gyrus	BA 10	3.82
[-27, 36, -15]	L orbito-frontal cortex	BA 11	3.61
[0, -51, 39]	precuneus	BA 7/31	3.96
[36, -42, -15]	R fusiform/lingual gyrus	BA 37	3.36
[0, -72, 6]	cuneus	BA 31	3.15
[-63, -54, 6]	L post. middle temporal gyrus	BA 37	3.90
[33, -12, -30]	R perirhinal cortex + inf. temporal gyrus	BA 28	3.80
[-33, -9, -30]	L perirhinal cortex	BA 28	3.75
[51, -6, -12]	R superior temporal sulcus	BA 21	3.22
[45, -48, -24]	R fusiform cortex	BA 37	3.25
Between-Subjects Ro-W			
[21, 24, 6]	R caudate head	—	3.58

W, wayfinding; T, trail following; Ro, route following; L, left; R, right; Inf., inferior; Post., posterior. All activations listed are statistically significant at the $p < 0.001$ level. For brevity, each activated region is listed only once; where several peaks were observed in the same region, the coordinates and Z scores refer to the strongest activation.

were examined; see Between Subjects W-Ro in Table 1. These include the perirhinal cortex bilaterally extending into the inferior temporal gyrus on the right (Figure 4B). Also shown in Figure 4B is a scattergram showing the correlation of performance and signal change for the peak voxel (33, -12, -30) and the corresponding voxel in the left temporal lobe. Hippocampal activation in this contrast also correlated positively with performance,

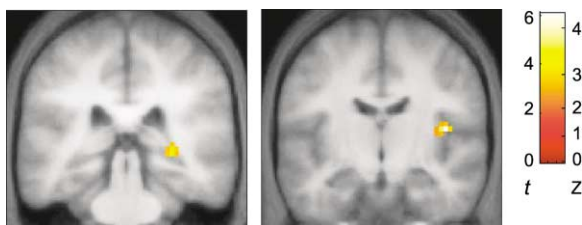


Figure 3. Within-Subjects Performance Effects
Two coronal sections through the normalized mean structural image showing regions reliably more active during accurate navigation than inaccurate navigation (in the wayfinding condition). (Left panel) Right posterior hippocampal activation (30, -33, -3). (Right panel) Right Insula (42, -12, 12). The regions shown here are thresholded at $p < 0.01$ to show the subthreshold extent of the activated region. The color bar indicates the t statistic associated with each voxel and Z score equivalent. Regions with volumes less than 10 voxels are not shown.

though not significantly so (e.g., $r = 0.52$, $p = 0.02$ at -27, -18, -18).

The opposite pattern (i.e., activation in wayfinding relative to route following that is negatively correlated with performance) was only seen in one region: the head of the right caudate, see Between Subjects RoW in Table 1. This region is shown in Figure 4C together with a scattergram showing the correlation of performance and signal change for the peak voxel (21, 24, 6). The same trend is seen in the right head of caudate for activation in wayfinding relative to trail following, although the correlation does not reach significance (e.g., $r = -0.64$; $p = 0.003$ at 15, 18, 6).

Discussion

Previous functional neuroimaging studies of navigation (e.g., Aguirre et al., 1996; Maguire et al., 1997, 1998a; Ghaem et al., 1997; Mellet et al., 2000; Grön et al., 2000; Pine et al., 2002; Shelton and Gabrieli, 2002) have not distinguished between wayfinding (finding novel paths between locations) and route following (following well-learned paths between locations). The current study explicitly distinguished between these forms of navigation and also made a related distinction between engagement with, and successful performance of, the task. The results show that activity in the right hippocampus was

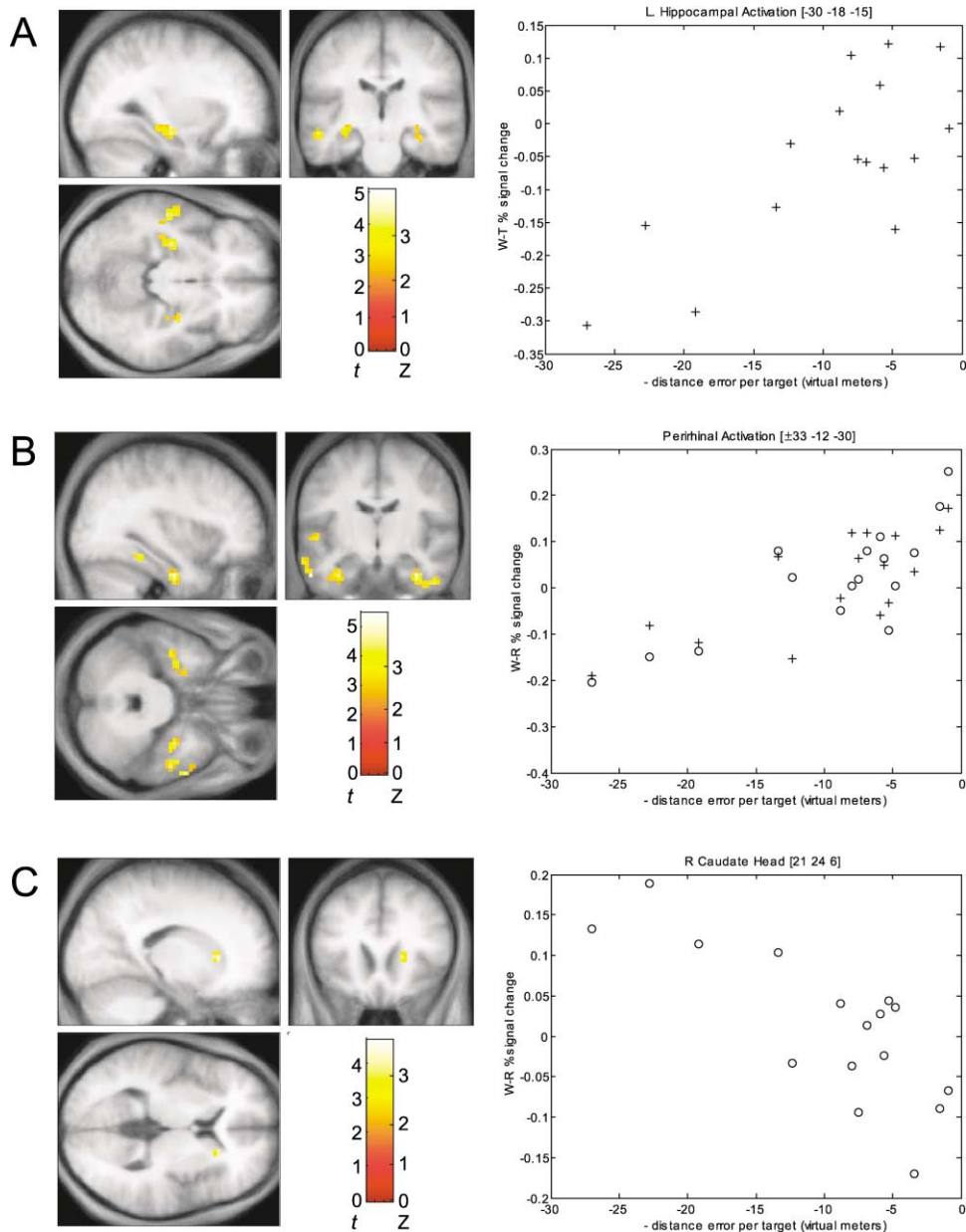


Figure 4. Between-Subjects Performance Effects

(A) The correlation between performance and activation during wayfinding relative to trail following. (Left) Sagittal, coronal, and axial sections showing the left hippocampal activation (−30, −18, −15), also showing the left inferior temporal lobe activation (−54, −21, −15). Note the subthreshold activation of the right hippocampus. (Right) Scattergram showing the correlation of individual performance and fMRI signal change between wayfinding and trail-following conditions for the peak voxel in the left hippocampus.

(B) The correlation between performance and activation during wayfinding relative to route following. (Left) The right perirhinal activation (33, −12, −30). The coronal and horizontal sections also show the corresponding contralateral activation (−33, −9, −30). (Right) Scattergram showing the correlation of performance and signal change between wayfinding and route-following conditions for the peak voxel in the right perirhinal cortex activation (indicated by “o” symbols) and the corresponding voxel in the left perirhinal cortex (indicated by “+” symbols).

(C) The correlation between performance and activation during route following relative to wayfinding. (Left) Activation of the right caudate head (21, 24, 6). (Right) Scattergram showing the correlation of performance and signal change between wayfinding and route-following conditions for the peak voxel in the right caudate head. Note: in each panel, the regions shown are thresholded at $p < 0.01$ to show the subthreshold extent of the activated region. The color bar indicates the t statistic associated with each voxel and Z score equivalent. Regions with volumes less than 10 voxels are not shown.

associated with accurate wayfinding within subjects. Beyond this, better navigators activated their hippocampi in wayfinding and the head of the right caudate in route following, while poorer navigators did not, sug-

gesting separable neural mechanisms underpinning accurate navigation in humans.

The present results are concordant with data from the neurophysiological literature that two distinct mecha-

nisms may support navigation (O'Keefe and Nadel, 1978; Cook and Kesner, 1988; Potegal, 1972; Morris et al., 1982; Packard and McGaugh, 1996; Morris et al., 1982). The first, place learning, is dependent on the hippocampus and permits the formation of a cognitive map that is flexible enough to facilitate navigation via a novel route. The second, response learning, is dependent on the caudate nucleus and supports an action-based representation that is inflexible (only supporting navigation via the same well-learned route) but which may have the advantage of mediating fast, automatic responses (see, for example, Poldrack et al., 2001).

If action-based and cognitive map representations are available in parallel (as suggested by the neurophysiological data; see, for example, Packard and McGaugh, 1996), the subject must select the appropriate representation for the task at hand. Performance would thus be expected to be strongly dependent upon which is used to guide behavior, and one might therefore expect different levels of performance to be associated with different patterns of activation in the brain. In particular, using an action-based representation in the wayfinding task will lead to poor performance because the routes learned in previous exposures to the environment will not correspond to the most direct route to the goal. Using a cognitive map representation when attempting a familiar route would not be expected to impair accuracy in this way (though it would increase the demand for perceptual processing and might thus adversely affect speed of travel). Below we discuss how the effects of between- and within-subjects variations in navigational performance on brain activations can be understood within this framework and how our results relate to previous studies.

Effects of Between-Subjects Variations in Performance

Accurate navigators showed greater hippocampal activation during wayfinding than poor navigators, as shown in the correlation between activation in wayfinding (relative to trail following) with subject's overall accuracy; see Figure 4A. This finding is consistent with the idea that the hippocampus supports accurate wayfinding. The correlation between individuals' accuracy and hippocampal activation in wayfinding relative to route following did not reach statistical significance, perhaps because good navigators also activate their hippocampus more than poor navigators in the route-following condition (for which there would be no adverse effect on the accuracy of the route in our account).

The right head of caudate showed a negative correlation between activation in wayfinding (relative to route following) and wayfinding accuracy ($r = -0.78$ at 21, 24, 6; $p < 0.001$, see Figure 4C). This is also consistent with our interpretation that good navigators select the appropriate representations for the task at hand, in this case, the caudate representation for route following. This interpretation is further corroborated by a post-hoc analysis of the relationship between accuracy and activation in the route-following task compared with trail following. This shows a significant positive correlation at the same voxel ($r = 0.47$ at 21, 24, 6; $p < 0.05$). We have also argued that selection of an action-based

representation when attempting a novel route will actually impair performance (rather than having a neutral effect). Consistent with this we note that in the poorest navigators, activation of the right head of caudate was greater during wayfinding than route following. This suggests that the correlation in Figure 4C is not driven solely by the beneficial effect of employing the appropriate representation for the task but also includes a contribution due to the cost of using an inappropriate representation.

A previous study (Maguire et al., 1998a) showed that activation of the anterior hippocampus (on the right) correlated with a related measure of performance (angular accuracy). Limitations of the PET methodology used made it impossible to determine whether this correlation was within or between subjects. Our analysis shows that individuals vary in the extent to which they engage the anterior hippocampus in the wayfinding task, and the best performing individuals are those in whom anterior hippocampal activation (relative to trail following) is strongest. The same study (Maguire et al., 1998a) also showed that activation of the right head of caudate during VR navigation correlated with the speed of navigation rather than its accuracy. Once again it was not possible to attribute this to within- or between-subjects variation. Our results suggest that this effect was largely due to a between-subjects effect and probably corresponded to use of familiar routes which could be followed at speed but which would not normally form the shortest path. To test our interpretation that the activation of the caudate observed by Maguire et al. (1998a) occurred due to fluent route following, we explicitly examined variations in subject's virtual speed. Consistent with our interpretation, fast route followers activated the right head of caudate while following routes (relative to trails) more than slow route followers did (e.g., $r = 0.69$, $p = 0.001$ at 6, 18, 3), while no such effect was found for wayfinding.

Our results may shed light on findings by Grön et al. (2000) who reported between-subjects differences in hippocampal activation during a VR navigation task. That study involved comparing a group of men with a group of women, the men activating the left hippocampus more than the women. However, women also performed significantly less well. As our results show that activation in the left hippocampus is correlated with performance in an exclusively male group, the sex differences seen by Grön et al. might be explicable in terms of a more general tendency for individual variations in performance to be correlated with hippocampal activation. This account leaves open the question of why the female group performed less well in Grön et al.'s study, and the possibility remains that the performance-related effects observed have a physiological basis that affects men and women differently (for instance, there are structural differences between the medial temporal lobes of men and women; Good et al., 2001).

The current results may also help to interpret the finding that two patients with extensive temporal lobe damage had apparently preserved spatial memory for a familiar neighborhood experienced many years before the lesion occurred (Teng and Squire, 1999; Rosenbaum et al., 2000). These cases may indicate that the spatial representation of an environment becomes independent

of the medial temporal lobe over time. However, it is also possible that the preserved performance in these patients depends in part on memory for familiar routes supported by the right caudate, where the hippocampus was only required at the initial stages of learning (i.e., before the routes became familiar).

The correlation between performance and activation of perirhinal cortex in the wayfinding condition relative to route following (Figure 4B) was another signature of good navigators. Recognition of new spatial scenes versus old ones has also been reported to activate this region (Rombouts et al., 2001). One possible interpretation of the perirhinal correlation we observe is that it reflects increased processing required to correctly identify the landmark locations from novel perspectives, a requirement of wayfinding but not route following.

Effects of Within-Subjects Variation in Performance

In addition to the between-subjects effects noted above, subjects (good and poor navigators alike) reliably activated the posterior right hippocampus when navigating accurately as opposed to inaccurately. However the hippocampus was not activated in performance-independent comparisons between wayfinding and trail following. This indicates that the hippocampus is specifically engaged in processes supporting accurate navigation, which might include determining where the goal is and computing the best route to it. In Maguire et al.'s (1998a) study, subjects were sometimes unable to find the target location. Posterior hippocampal activity was observed in successful compared with unsuccessful navigation trials. We have extended those findings by showing that right posterior hippocampal activation is parametrically related to within-subject variations in the accuracy of navigation.

This relationship allows us to address a puzzle regarding experience-related structural change in the hippocampus. Increases in posterior hippocampal volume have been associated with prolonged experience of navigation in London taxi drivers (Maguire et al., 2000), yet in the general population, variation in navigational expertise alone does not correlate with structural changes (Maguire et al., 2003). Our observation of posterior hippocampal activation specific to accurate navigation within subjects suggests the possibility that the structural changes could result from increased activation which would presumably be maintained over many years of navigational experience in taxi drivers.

The insula was also activated in accurate as opposed to inaccurate navigation. Activation of the insula has previously been linked to imagined body movements in a mental navigation task (Ghaem et al., 1997). This function may relate to its role in the relay of somatosensory information to the limbic system (Mesulam and Mufson, 1982), in vestibular processing (Bottini et al., 2001), and in crossmodal interactions of visual and vestibular inputs (Dieterich et al., 1998; Brandt et al., 1998). In the absence of vestibular and somatosensory input, accurate navigation in our VR paradigm requires subjects to take the purely visual stimulus and imagine themselves moving bodily in the virtual space. The insula activation may thus reflect a richer crossmodal con-

struct of bodily motion, or greater use of it, during accurate navigation.

The Extended Navigation Network

The performance-related effects noted above may explain some discrepancies between the results of previous studies of navigation. For instance, some show activation extending into the hippocampus (e.g., Maguire et al., 1998a; Ghaem et al., 1997; Grön et al., 2000; Pine et al., 2002), while others do not (Aguirre et al., 1996; Maguire et al., 1998b). Our results suggest that such discrepancies could arise from subtle differences between the experimental tasks, especially the degree to which they could be solved using memory for well-learned routes, and from differences in the overall level of performance achieved by different subject groups. Such differences aside, there is general agreement between the results of previous neuroimaging studies relating to navigation (see Burgess et al., 2002; Maguire et al., 1999, for reviews; and subsequent papers, e.g., Shelton and Gabrieli, 2002), showing a consistent network of brain regions is activated during navigation, including the precuneus, retrosplenial, posterior parietal, fusiform, and parahippocampal cortices. In many previous studies, performance was not analyzed or was included only as a subsidiary analysis. Our study indicates that, in contrast to the hippocampus, this network is engaged by any attempt to perform wayfinding, regardless of success. Our interpretation is that these regions are engaged in processes that, while involved in any attempt at wayfinding, are not sufficient for accurate navigation.

These processes might include perceptual processing required to establish and maintain one's bearings (e.g., interpreting the visual scene such that one can identify a familiar landmark and thus locate oneself with reference to it). Previous studies suggest that such spatial processing of the visual scene involves the posterior parahippocampal and fusiform cortices (O'Craven and Kanwisher, 2000; Epstein and Kanwisher, 1998; Aguirre and D'Esposito, 1997). In our study, these regions showed the strongest cortical activations in performance-independent comparisons between wayfinding and the other conditions. This contrasts with more anterior regions (i.e., perirhinal cortex and anterior hippocampus) that are only engaged in good navigators.

Other regions activated in performance-independent comparisons between wayfinding and route following and between wayfinding and trail following include the posterior parietal cortex, retrosplenial cortex, and precuneus. These regions have been implicated in retrieval of imageable information from memory (Fletcher et al., 1996) and in the transformations of reference frame that may be entailed in this process (Burgess et al., 2001, 2002). Medial prefrontal activation was specific to the wayfinding task. This might relate to executive functions involved in planning novel routes, as a similar region was associated with navigation when a familiar route was blocked by a novel barrier (Maguire et al., 1998a).

The route-following condition (when compared to the trail-following condition) activated a much less extensive network involving the caudate body and insula and additionally (in comparison with wayfinding) lateral pari-

etal/somatosensory cortex, premotor and motor cortices, and SMA. This network we interpret as being responsible for maintaining, retrieving, and acting upon a predominantly action-based representation of the well-learned route. This is sufficient to produce excellent performance on the task, without the same degree of perceptual processing required in the wayfinding task. The body of the caudate nucleus (bilaterally) was activated in both wayfinding and route following (relative to trail following). This contrasts with the performance-related activation of the right head of the caudate and suggests that the body of the caudate plays a more general role in navigation.

Lateralization of Function

The overall network activated in attempting the wayfinding task shows a noticeable lateralization, with the strongest and most extensive cortical activations on the right (see the lingual, fusiform, parahippocampal, and prefrontal cortices in Figure 2A), consistent with neuropsychological data (Smith and Milner, 1981; Abrahams et al., 1997; Epstein et al., 2001; Spiers et al., 2001b; see Burgess et al., 2002, for further discussion).

The lateralization of functions specifically associated with accurate navigation is more complex. Maguire et al. (1998a) found that performance-related effects in the right hippocampus and bilateral activation was seen in a straightforward comparison of successful and unsuccessful trials; however, they could not distinguish between within- and between-subjects effects. The current results and those of Grön et al. (2000) suggest that different patterns of lateralization apply to within- and between-subjects effects. In the current study, the within-subjects effect of performance implicated the right hippocampus and right insula in accurate navigation. However, the between-subjects effects of performance show, if anything, a left asymmetry. For instance, the correlation of activation with performance is stronger in the left hippocampus than the right. Grön et al. (2000) found a similar between-subjects pattern: while right medial temporal regions were active irrespective of the subject's sex, group differences (which we argue may be related to performance) were apparent in the activation of the left hippocampus. The pattern seen in both studies is consistent with an overall right lateralization of hippocampal function (the within-subjects effects), with a more bilateral pattern in better navigators (making activation in the left hippocampus more strongly correlated with between-subjects variation in performance).

Conclusions

Neurophysiological studies involving rodents have shown that wayfinding and route following involve different forms of representation with correspondingly distinct neural bases (Potegal, 1972; O'Keefe and Nadel, 1978; Morris et al., 1982; Packard and McGaugh, 1996). In the current study, we found evidence that a similar distinction is observed in the human brain.

The hippocampus is specifically involved in accurate navigation via new routes, suggesting that it provides a cognitive map, whereas good navigators activate the head of the right caudate nucleus when following well-learned routes. Wayfinding behavior also involves per-

ceptual-spatial processing not directly related to variations in performance. In comparison with trail following, this processing engages a network of regions, including precuneus, posterior parietal, retrosplenial, parahippocampal and fusiform cortices, and caudate body. By contrast, route following engages a largely separate network, including insula, caudate body, and (in comparisons with wayfinding) lateral parietal/somatosensory cortex, premotor cortex, and SMA. The almost complete absence of medial temporal lobe, occipital, and posterior parietal regions in this network suggests that, through repeated rehearsal, a predominantly action-based representation of the route is formed, reducing the demand for perceptual-spatial processing during navigation. The route-following network may thus act like an autopilot, freeing cognitive resources for other tasks. In summary, whether following a well-worn route or finding a path less traveled, successful navigation depends on activation of the appropriate neural substrate.

Experimental Procedures

Subjects

Sixteen healthy right-handed male volunteers participated (mean age, 28.9 years; range, 23.0–40.3 years). All participants gave informed written consent in accordance with requirements of the local medical ethics committee. All had previous experience of playing first-person videogames.

Virtual Environments

Two distinctive virtual towns (see Figure 1) were constructed using the Quole map editor (Lithium Software). Each town contained nine scattered landmark locations (e.g., shops, cafes) that were clearly identifiable and distinct from one another. The towns were approximately the same size and, despite surface differences that made them visually distinctive, had similar topology in that they contained a similar number of roadways and junctions.

Veridical 2D maps of the towns taken from the map editor were used to calculate "ideal paths" between each pair of landmark locations, using a resistive grid algorithm (based on methods similar to those described in Bugmann et al., 1994). The ideal path was the most direct route between landmarks allowing reasonable clearance of obstacles. These ideal paths were used both to assess subjects' performance and, where necessary, to produce visible trails indicating the correct path between landmark locations (i.e., in the trail-following condition and in training for the route-following condition, both described below).

A modified version of the Quake2 video game (id Software) was used to present subjects with a ground-level first-person perspective view of the towns. Subjects moved around the virtual environment using their right hand to operate specified keys to move forward or backward and turn left or right.

Pre-Scan Training

To acquire knowledge about the topography of the two towns and to prepare them for the experimental tasks during scanning, subjects were trained immediately prior to scanning at a desktop computer.

In Town 1, subjects were allowed to explore freely for 15 min. Occasional verbal direction from an experimenter was necessary to ensure (1) that the subjects attended to the landmark locations, (2) that each location was visited on more than one occasion and approached from more than one direction, and (3) that all the roadways were fully explored.

In Town 2, subjects were trained to follow a prescribed route, later used in the experimental route-following task and described in more detail below (see Experimental Tasks). The route was initially indicated by a trail of closely spaced green blobs following the shortest path between landmark locations and just below eye level.

Subjects followed the trail, and an experimenter drew the target locations to their attention as they were encountered. On reaching the end of the route (having navigated to eight successive target locations), the display was cleared, and after a short delay the scene faded in with the subjects returned to the starting point, to begin following it again. The spacing between the guiding markers was increased with each repetition of the route so that subjects were increasingly reliant on the memory for the route and the target images. Eventually, the trail was removed completely. Subjects then continued to follow the route until they had spent a total of 15 min in the town.

Note that the towns used for the different tasks were counterbalanced between subjects, as was the order in which the subjects were trained (free exploration first, route following first).

Experimental Tasks

During fMRI scanning, the experimental conditions used three variants of a cued navigation task, similar to that employed in previous studies (Maguire et al., 1998a; Spiers et al., 2001a, 2001b). In all three experimental conditions (described in detail below), subjects were presented with a first-person perspective of a virtual-reality town and moved through it as described above. In each case, correct performance corresponded to moving between pairs of landmark locations by the shortest route.

For the navigation conditions (“wayfinding” and “route following”), a static image in the lower right part of the display showed the current target location throughout. Subjects thus did not have to store a representation of the current target location while they were navigating, an advance over Maguire et al. (1998a). The subject was instructed to navigate to the indicated location (strictly the place from which the image was captured), the only difference between the tasks being the nature of their prior experience in the environment. In the third experimental condition, subjects simply followed a visible trail to the goal location. Figure 1 depicts examples of the tasks.

Wayfinding

Subjects had to find their way between target locations in Town 1. Each sequence of target locations used one landmark location as its starting point and the remaining eight as successive targets. A novel sequence of target locations was used each time the subject performed the task. The sequence was chosen so that a given pairing of start point and destination was never repeated during the experiment. Each new target would thus require the subject to follow a relatively unfamiliar path that they had not previously been required to follow in its entirety. Good performance would require global knowledge of the layout of the town, including the spatial relationships of the scattered landmark locations (i.e., a cognitive map). Knowledge of familiar routes would not lead to good performance, since the shortest paths between the arbitrarily chosen target locations rarely if ever involved repeating the same route over any great distance.

Route Following

Subjects repeatedly followed the same route in Town 2, i.e., the same fixed sequence between nine target locations they had been trained on was used each time the subject performed the task. One landmark acted as the starting point for the route, the eight remaining target locations were visited in fixed sequence. The sequence was chosen so that in traveling to each target location the subject did not pass another landmark en route. Note that this constraint also made the distance between adjacent landmarks in the prescribed route somewhat shorter than the average distance between pairs of landmarks used in the other conditions. Because of the design of the town, subjects also had little opportunity to see any of the landmarks other than the current target. This was intended to restrict their ability to gauge spatial relationships of target locations not adjacent to one another in the prescribed route, thus inhibiting the development of a cognitive map type representation. Subjects could perform the task effectively using only local knowledge of the familiar relationships between adjacent locations in the prescribed route and/or a representation of the repeated pattern of movements required to complete the route.

Trail Following

This task was identical to the wayfinding task, except that instead of target images, a trail of green markers just below eye level indi-

cated the shortest path to the next target location. Subjects simply had to follow this trail and did not require any knowledge of the environment to do so.

The experimental tasks were presented in 50 s epochs. The time allowed was just sufficient to complete the shortest eight-target route if the subject navigated optimally. At the end of each epoch, a message indicating the next task was displayed briefly (~2.4 s) against a black background, after which the first target image was displayed (in navigation conditions) and the scene simultaneously faded in (~1.5 s), with the subject moved to the appropriate starting location for the next epoch. Subjects completed eight blocks, where each block comprised one epoch of each task followed by a 50 s rest period during which the display was black, and no response was required. Within each block, the experimental tasks appeared in pseudorandom sequence, where each subject had the same sequence of conditions. Virtual movements were logged throughout the experiment at 0.1 s intervals. These records were used to calculate mean speed of movement, rate and direction of turn, which were incorporated into the fMRI analysis (see below). The path traveled by the subject was compared with the “ideal” path, accuracy being measured by subtracting the length of the ideal path between each pair of landmarks from the length of the path traveled (“distance error”). As the ideal paths incorporated reasonable clearance around obstacles, it was possible to get a small negative score for distance error by “cutting corners.” This measure is an improvement on the angular accuracy measure used by Maguire et al. (1998a), since it takes account of variations in the best available path to each goal due to the layout of the town.

Image Acquisition and Data Analysis

Data were acquired using a 2 Tesla Siemens Magnetom VISION whole body MRI system (Siemens GmbH, Erlangen, Germany) equipped with a head volume coil. A structural MRI scan using a standard three-dimensional T1 weighted sequence was acquired from each subject. Functional T2*-weighted images were obtained using echo-planar imaging (echo time (TE) = 40 ms). Volumes were acquired continuously for the whole head: 32 slices, each 3 mm thick, 3.2 s per volume. Image analysis was performed using SPM99 (Wellcome Department of Imaging Neuroscience, London, UK; Friston et al., 1995) in a standard manner. Briefly, the functional images were realigned (with each other) and coregistered with the structural scan. The images were normalized to a standard template (Montreal Neurological Institute) and spatially smoothed with a Gaussian filter (6 mm full width half maximum). For each individual, the fMRI time series was high-pass filtered (minimum cutoff period 167 s) and modeled as the weighted sum of regressors corresponding to effects of interest and potentially confounding factors (which were thus prevented from affecting the parameters estimated for the effects of interest). The effects of interest were condition (wayfinding, route following, trail following, rest) and time-dependent effects of performance in the wayfinding condition (distance error in navigating to each target). The other regressors included in the model were effects of movement in VR space (rate and direction of turn, forward speed) and event-related effects corresponding to the appearance of each new target image or trail. All the above regressors were convolved with the canonical hemodynamic response function. Finally, the model also included regressors based on estimates of head movement obtained from the realignment procedure (to account for any second-order effect of such movement remaining after realignment). The weights for the best fitting model were found and subjected to a random effects analysis. That is, for each voxel in the brain, single sample t tests were used to determine whether the estimated contrast of parameter estimates (i.e., weights) between conditions (e.g., wayfinding–route following) was significantly different from zero. We also performed correlations of activation in contrasts involving the wayfinding condition with a measure of each individual’s overall performance in the wayfinding task (the average distance error in navigating to each target). Except where indicated, the results we report exceed a threshold for statistical significance of $p < 0.001$ (uncorrected for multiple comparisons—given our interest in brain areas specified in advance, i.e., hippocampus and caudate, and areas reported in previous neuroimaging studies; Aguirre et al., 1996; Ghaem et al., 1997; Maguire et al., 1997, 1998a).

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