

Reference Frames for Spatial Cognition: Different Brain Areas are Involved in Viewer-, Object-, and Landmark-Centered Judgments About Object Location

Giorgia Committeri^{1,2}, Gaspare Galati^{2,3}, Anne-Lise Paradis^{1,4},
Luigi Pizzamiglio^{2,5}, Alain Berthoz⁴, and Denis LeBihan¹

Abstract

■ Functional magnetic resonance imaging was used to compare the neural correlates of three different types of spatial coding, which are implicated in crucial cognitive functions of our everyday life, such as visuomotor coordination and orientation in topographical space. By manipulating the requested spatial reference during a task of relative distance estimation, we directly compared viewer-centered, object-centered, and landmark-centered spatial coding of the same realistic 3-D information. Common activation was found in bilateral parietal, occipital, and right frontal premotor regions.

The retrosplenial and ventromedial occipital–temporal cortex (and parts of the parietal and occipital cortex) were significantly more activated during the landmark-centered condition. The ventrolateral occipital–temporal cortex was particularly involved in object-centered coding. Results strongly demonstrate that viewer-centered (egocentric) coding is restricted to the dorsal stream and connected frontal regions, whereas a coding centered on external references requires both dorsal and ventral regions, depending on the reference being a movable object or a landmark. ■

INTRODUCTION

Spatial locations may be defined either relative to the viewer or relative to some external reference (Howard, 1982). In the first case, spatial locations are coded egocentrically, with reference to relevant body parts, such as the eyes, head, trunk, and/or arm. This kind of coding is highly dynamic, needs continuous updating as one moves, and is particularly useful for the organization of movements towards objects in space. External references, instead, are used, for example, in object-based representations, which describe the spatial relationships among the component parts of an object or the relative position of multiple objects. Another common example comes from the study of spatial orientation and navigation in humans and animals. Generally speaking, memory for places and way-finding are processes that are easier to understand in terms of coordinates external to the viewer, or allocentric (Berthoz, 1997). Indeed, most accounts of spatial orientation include some kind of enduring storage of environmental information, in the form of internal geocentric “cognitive maps” of topographical space (O’Keefe & Nadel, 1978), or of modules

for the permanent storage of the geometrical structure of spatial layouts (Wang & Spelke, 2002).

Egocentric frames are typically associated with the posterior parietal cortex. Neurons coding spatial position relative to body parts have been found in the monkey’s posterior parietal cortex and in connected regions of the premotor cortex (Cohen & Andersen, 2002; Colby, 1998). Patients with lesions to the posterior parietal cortex may either show inaccurate visuomotor coordination (optic ataxia: Perenin & Vighetto, 1988) or fail to explore the contralesional side of space (unilateral neglect: Vallar, 1998). In unilateral neglect, the affected sector of space is usually egocentrically defined (see Bisiach, 1997; Vallar, Guariglia, & Rusconi, 1997, for related demonstrations). Both ataxic and neglect patients show specific deficits in perceiving the position of their body midsagittal plane (Pizzamiglio, Committeri, Galati, & Patria, 2000; Perenin, 1997), a fundamental egocentric spatial principle (Jeannerod & Biguer, 1989). A series of neuroimaging studies has provided direct evidence of the involvement of parietal–frontal circuits in the egocentric coding of space. A posterior parietal–frontal premotor network, bilateral but more extensive on the right, is activated when stimuli are localized with respect to the body midsagittal plane (Vallar et al., 1999). This activation is much larger than when an object-based judgement is performed on the same stimuli (Galati, Lobel, et al., 2000), and is found for body-centered

¹SHEJ/CEA, Orsay, France, ²Fondazione Santa Lucia, Rome, Italy, ³University G. d’Annunzio, Chieti, Italy, ⁴CNRS—Collège de France, Paris, France, ⁵University of Rome La Sapienza, Italy

localization of both visual and tactile stimuli (Galati, Committeri, Sanes, & Pizzamiglio, 2001).

Object-based coding of space has been much less studied. Its existence has been demonstrated in the monkey's frontal lobe (Olson & Gettner, 1995). In humans, unilateral neglect may concern the contralesional side of individual objects, independent of their egocentric position ("object-based neglect": Driver, 1999). Several neuroimaging studies (Fink, Marshall, Shah, et al., 2000; Galati, Lobel, et al., 2000; Honda, Wise, Weeks, Deiber, & Hallett, 1998; Fink, Dolan, Halligan, Marshall, & Frith, 1997) have found activation in the posterior parietal cortex and the dorsal premotor cortex (PMD), mainly in the right hemisphere, and in early visual processing areas, during object-based spatial judgements.

Finally, coding of topographical space is typically associated with the hippocampal formation. Cells with allocentric properties have been found in the hippocampal formation of both freely-moving rats (Taube, Muller, & Ranck, 1990; O'Keefe & Dostrovsky, 1971) and monkeys (Rolls & O'Mara, 1995; Ono, Nakamura, Nishijo, & Eifuku, 1993), as well as in the rat retrosplenial cortex (Chen, Lin, Green, Barnes, & McNaughton, 1994; McNaughton, Leonard, & Chen, 1989), but also in the monkey's posterior parietal cortex (Snyder, Grieve, Brotchie, & Andersen, 1998). In humans, ventromedial lesions encroaching on the parahippocampal gyrus (Aguirre & D'Esposito, 1999; Habib & Sirigu, 1987) or the hippocampus proper (Spiers, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2001) lead to difficulties in storing and/or recalling identity and spatial location of important landmarks, resulting in topographical disorientation in new and/or familiar environments. Also patients with retrosplenial lesions are unable to orient themselves and to know which direction to take, as if they had lost their "heading" within the environment (Aguirre & D'Esposito, 1999).

Neuroimaging studies using a variety of topographical tasks, such as landmark knowledge, orientation in large-scale space and navigation, have detected activation in the posterior parahippocampal cortex (e.g., Gron, Wunderlich, Spitzer, Tomczak, & Riepe, 2000; Mellet et al., 2000; Maguire, Frith, Burgess, Donnett, & O'Keefe, 1998; Aguirre & D'Esposito, 1997; Ghaem et al., 1997; Maguire, Frackowiak, & Frith, 1997; Aguirre, Detre, Alsop, & D'Esposito, 1996), the hippocampus (Gron et al., 2000; Ghaem et al., 1997; Maguire, Frackowiak, & Frith, 1996, 1997), and the retrosplenial cortex (reviewed by Maguire, 2001), as well as the posterior parietal cortex (e.g., Gron et al., 2000; Mellet et al., 2000; Aguirre, Detre, et al., 1996). Such complex tasks entail spatial operations referred both to the viewer and to external references, which are difficult to disentangle. However, taking into account the subject's navigational strategy, recent studies were able to show that different regions are involved when subjects use different spatial

references: for example, the hippocampus is involved only when subjects rely on multiple landmarks available in the environment and their spatial relationships, and not when they use automatic stimulus-response associations (Hartley, Maguire, Spiers, & Burgess, 2003; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003).

In summary, there is evidence that distinct neural structures are involved depending on the spatial references employed during various spatial operations. The aim of the present study was to directly compare viewer-centered, object-centered, and landmark-centered spatial coding of the same realistic three-dimensional information, by using a simple perceptual task, which allows to explicitly manipulate the employed spatial reference. We built a 3-D virtual environment representing a square arena in a park, with some relevant landmarks such as a three-winged palace and a fountain (see Figure 1, central frame). Then, we took snapshots of the environment taken from different points of view (see examples of stimuli in Figure 1). Each snapshot included a partial view of the spatial layout and three additional objects: two target objects (the garbage cans) and one reference object (the red ball). Before entering the scanner, participants were shown animations simulating rapid circular walks in the environment, in order to familiarize with it. Then, they were shown the 12 possible points of view, they were instructed about tasks, and finally they were trained until the achievement of a good performance.

Functional magnetic resonance images were acquired while subjects judged, for each snapshot, which of the two target objects was closer either to the observer (viewer-centered condition), or to the reference object (object-centered condition), or to the central wing of the palace (landmark-centered condition). A common control task was also used, where subjects judged which of the two target objects was laying on the ground. Importantly, the three reference frames were independently manipulated: In each trial, the point of view (viewer's position) was independently moved, and the position of the target and reference objects were independently changed, both with respect to the viewer and the environment (check examples in Figure 1). Thus, for example, when judging about the relative position of the two target objects with respect to the observer (viewer-centered condition), both the object- and landmark-relative positions of the two objects were completely irrelevant. The same holds for the object- and landmark-centered conditions.

A further important feature of this paradigm is that, in both the viewer- and object-centered conditions, the spatial reference (i.e., the point of view and the reference object, respectively) did not have a fixed position in the environment. Thus, an enduring representation of the environment structure did not help. Crucially, instead, the landmark-centered condition required to access a mental reconstruction of the overall

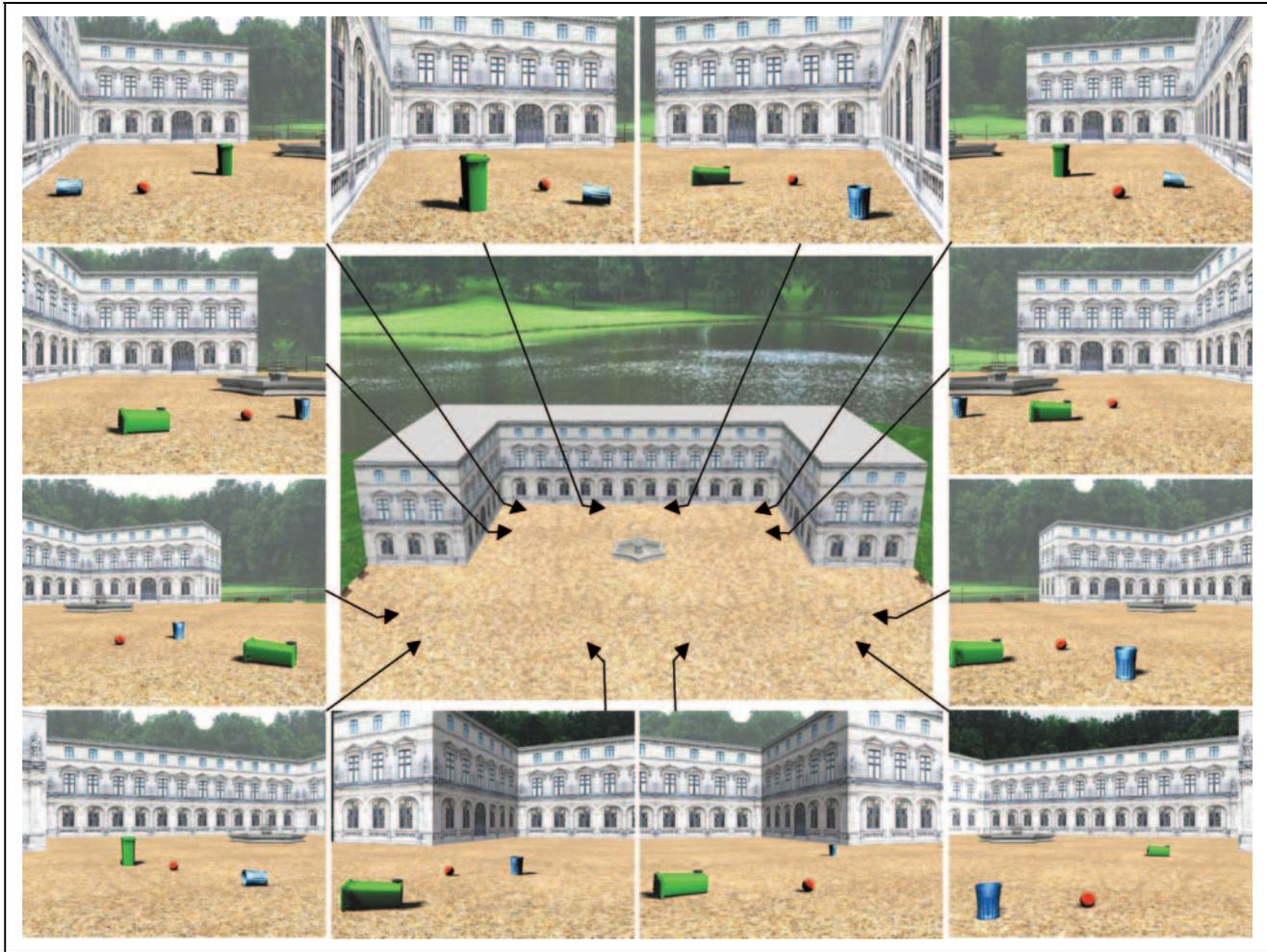


Figure 1. 3-D virtual environment and examples of stimuli. The central frame shows an aerial view of the environment and the position of the 12 cameras (black arrows). The small frames all around are examples of stimuli, one for each point of view. Note that each point of view includes a partial view of the central wing of the palace. Note also that the two target objects (the blue and the green garbage cans) and the reference object (the red ball) are presented in different positions both relative to the observer and in the environment. Either of the two garbage cans is lying on the ground.

environmental geometry: the spatial reference (the central wing of the palace), in fact, had to be recognized by means of its geometrical relationships with the lateral wings and the rest of the environment.

RESULTS

Errors and Response Times

Psychophysical data were successfully collected from 12 of the 14 scanned subjects. Error rates were 5% in the viewer-centered condition, 3% in the object-centered condition, 5% in the landmark-centered condition, and 3.5% in the control task. Differences were not significant. Response times were significantly faster in the control task than in any of the three spatial conditions, but there were no differences between the spatial conditions (mean response times: 981 msec in the viewer-centered condition, 982 msec in the object-

centered condition, 964 msec in the landmark-centered condition, 932 msec in the control task).

Activation Observed for Each Spatial Condition Relative to the Control Task

When we compared the three spatial conditions to the control task, we detected a set of regions that were activated by all (posterior parietal and premotor cortex), and other regions that were activated by only one spatial condition (ventrolateral and ventromedial occipital-temporal cortex, left ventral premotor cortex [PMv]). All activated regions are listed in Table 1 and shown in Figure 2.

Parietal regions were activated by all spatial conditions and included the lateral and medial posterior parietal cortex, extending posteriorly to the occipital lobe. On the lateral cerebral surface, most of the activation was

Table 1. Activation Observed for Each Spatial Condition

<i>Region</i>	<i>Viewer-centered</i>	<i>Object-centered</i>	<i>Landmark-centered</i>
Right parietal–occipital	Right superior parietal lobule ($z = 5.01$) (16, -74, 60) (BA 7)	Right superior parietal lobule ($z = 3.84$) (28, -70, 56) (BA 7)	Right superior parietal lobule ($z = 4.57$) (16, -82, 52) (BA 7)
	Right superior occipital gyrus ($z = 4.68$) (24, -82, 20) (BA 19)	Right superior occipital gyrus ($z = 5.39$) (28, -78, 32) (BA 19)	Right superior occipital gyrus (24, -82, 20) (BA 19)
	Right middle occipital gyrus ($z = 4.7$) (32, -82, 36) (BA 19)	Right middle occipital gyrus (32, -82, 36) (BA 19)	Right middle occipital gyrus ($z = 4.55$) (36, -86, 28) (BA 19)
	Right dorsal precuneus ($z = 4.29$) (4, -66, 60) (BA 7)	Right dorsal precuneus ($z = 5.1$) (16, -78, 48) (BA 7)	Right dorsal precuneus (16, -78, 48) (BA 7)
	Right cuneus ($z = 3.97$) (16, -78, 44) (BA 18/19)	Right cuneus (16, -78, 44) (BA 18/19)	Right cuneus (16, -78, 44) (BA 18/19)
			Right inferior parietal lobule ($z = 3.36$) (36, -54, 52) (BA 40)
		Right ventral precuneus (24, -62, 20) (BA 23)	Right ventral precuneus (24, -62, 20) (BA 23)
Left parietal–occipital			Right retrosplenial (posterior cingulate) (9, -48, 9) (BA 30)
			Right anterior calcarine (20, -38, -4)
	Left superior parietal lobule ($z = 4.05$) (-24, -78, 52) (BA 7)	Left superior parietal lobule ($z = 2.88$) (-20, -74, 52) (BA 7)	Left superior parietal lobule ($z = 4.57$) (-20, -74, 56) (BA 7)
	Left dorsal precuneus ($z = 3.83$) (-4, -66, 60) (BA 7)	Left dorsal precuneus (-4, -66, 60) (BA 7)	Left dorsal precuneus (-4, -66, 60) (BA 7)
	Left middle occipital gyrus (-28, -78, 28) (BA 19)	Left middle occipital gyrus ($z = 4.1$) (-28, -78, 28) (BA 19)	Left middle occipital gyrus ($z = 4.98$) (-32, -90, 28) (BA 19)
	Left superior occipital gyrus ($z = 3.99$) (-20, -70, 28) (BA 19)	Left superior occipital gyrus (-20, -70, 28) (BA 19)	Left superior occipital gyrus (-20, -70, 28) (BA 19)
			Left cuneus (-16, -66, 16) (BA 18)
		Left anterior calcarine (-16, -46, 0)	

Right superior frontal	Right superior frontal/precentral sulcus ($z = 3.93$) (20, 2, 56) (BA 6)		Right superior frontal/precentral sulcus ($z = 3.86$) (24, -6, 56) (BA 6)
	Right superior frontal gyrus/sulcus ($z = 2.71$) (28, 10, 60) (BA 6/8)		Right superior frontal gyrus/sulcus ($z = 4.5$) (24, 10, 56) (BA 6/8)
	Right middle frontal gyrus (28, 6, 52) (BA 8)		Right middle frontal gyrus (32, 18, 52) (BA 8)
Right inferior frontal	Right inferior frontal gyrus (triangular) ($z = 3.64$) (48, 14, 24) (BA 45)		Right inferior frontal gyrus (triangular) (48, 14, 24) (BA 45)
	Right inferior frontal gyrus (opercular) ($z = 2.8$) (36, 2, 28) (BA 44)	Right inferior frontal gyrus (opercular) ($z = 3.48$) (52, 10, 24) (BA 44)	Right inferior frontal gyrus (opercular) ($z = 2.97$) (48, 10, 20) (BA 44)
		Right precentral gyrus ($z = 3.03$) (48, 6, 32) (BA 6)	Right precentral gyrus ($z = 2.99$) (52, 6, 32) (BA 6)
Left inferior frontal	Left inferior frontal gyrus (triangular) ($z = 3.3$) (-44, 26, 28) (BA 45)		
	Left inferior frontal gyrus (opercular) ($z = 4.4$) (-36, 14, 32) (BA 44)		
Right lateral occipital-temporal		Right inferior temporal gyrus ($z = 3.97$) (48, -58, -16) (BA 37)	
Left lateral occipital-temporal		Left inferior occipital gyrus ($z = 3.72$) (-44, -78, -8) (BA 18)	
Right medial occipital-temporal			Right lingual gyrus ($z = 3.28$) (12, -86, -12) (BA 18/19)
			Right fusiform gyrus ($z = 4.26$) (28, -78, -8) (BA 37)
			Right parahippocampal gyrus (32, -38, -12)
Left medial occipital-temporal			Left lingual gyrus (-24, -58, -12) (BA 18/19)
			Left fusiform gyrus ($z = 4.46$) (-20, -46, -12) (BA 37)
			Left parahippocampal gyrus (-32, -38, -8)

Table shows regions activated for each spatial condition relative to the control task. For each region, the different anatomical areas involved are listed (Tzourio-Mazoyer, 2002; Duvernoy, 1991). For each anatomical label, coordinates in MNI space and Brodmann's areas (Talairach and Tournoux, 1988) are given for voxels representing local maxima of activation or for representative voxels. In the former case, z -values are also provided.

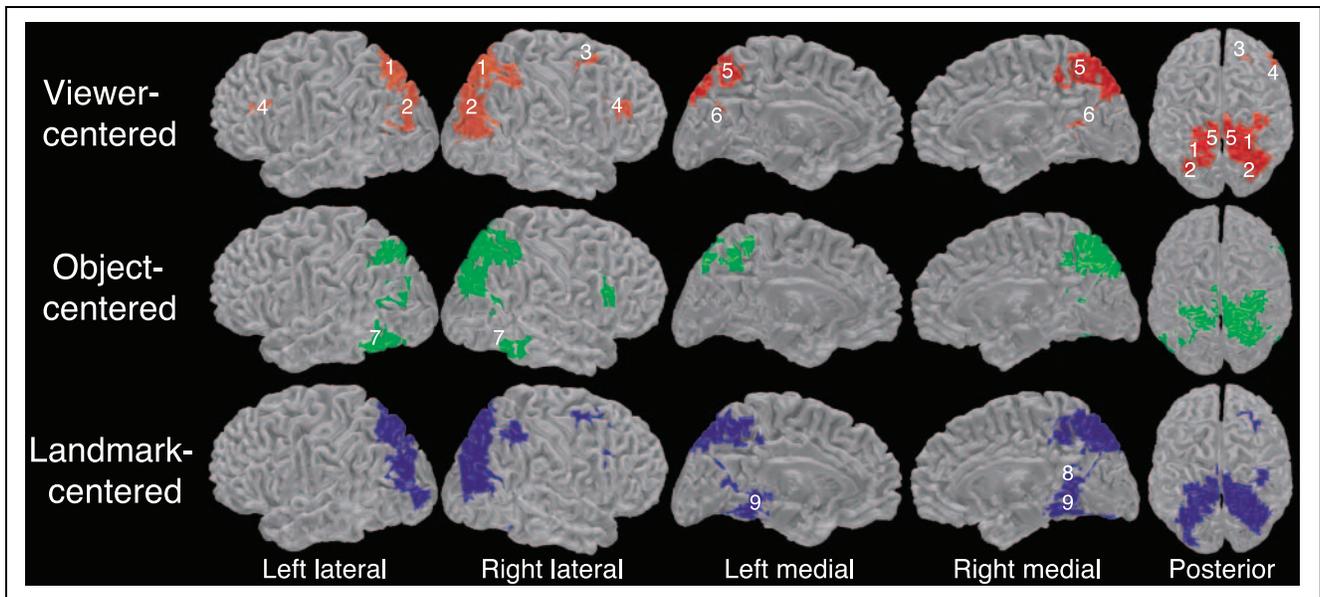


Figure 2. Activation observed for each spatial condition relative to the control task. Color labels refer to the viewer-centered (red), the object-centered (green), and the landmark-centered (blue) conditions. Lateral, medial, and posterior three-dimensional views of a standard brain are shown. Numbers indicate different anatomical regions: 1 = superior parietal lobule, 2 = superior and middle occipital gyri, 3 = superior frontal sulcus/superior precentral sulcus, 4 = inferior frontal sulcus/inferior precentral sulcus, 5 = dorsal precuneus, 6 = parietal–occipital sulcus, 7 = lateral occipital–temporal, 8 = retrosplenial (posterior cingulate), 9 = medial occipital–temporal (fusiform, lingual, and posterior parahippocampal gyrus).

located inside the horizontal and descending segments of the intraparietal sulcus, ventrally becoming the intra-occipital sulcus. The activation involved the superior parietal lobules and both the superior and middle occipital gyri. A small portion of the right inferior parietal lobule was also activated during the landmark-centered condition. On the medial cerebral surface, the activation encompassed the precuneus, a small region of the cuneus, and the superior portion of the parietal–occipital sulcus. In the landmark-centered condition, it comprised the parietal–occipital sulci in their whole extension, reaching ventrally the anterior calcarine sulci, and a portion of the posterior cingulate (i.e., the retrosplenial cortex) on the right. In the viewer-centered and object-centered conditions, instead, the medial activation was quite asymmetrical, and reached the ventral end of the parietal–occipital sulcus only in the right hemisphere.

In the frontal lobe, we found a right ventrolateral cluster, centered in the posterior portion of the inferior frontal sulcus, near the junction with the inferior precentral sulcus. This region was activated by all three spatial conditions, but a slight anterior–posterior separation was evident between the viewer-centered and the object-centered activation, with the former including the pars opercularis (BA 44) and the pars triangularis (BA 45) of the inferior frontal gyrus (IFG), whereas the latter was restricted to the precentral gyrus and the pars opercularis of the IFG. The viewer-centered condition also elicited significant activity in a symmet-

ric region of the left hemisphere. A further frontal region was detected dorsolaterally in the right hemisphere, for the viewer-centered and the landmark-centered conditions. It was centered in the posterior portion of the superior frontal sulcus (SFS), near and anteriorly to the junction with the superior precentral sulcus.

A bilateral ventrolateral occipital–temporal region was activated only by the object-centered condition. In the right hemisphere, the activation was centered in the inferior temporal gyrus, whereas in the left hemisphere it was centered slightly more posteriorly in the inferior occipital gyrus.

Finally, a ventromedial occipital–temporal region was activated in both hemispheres only in the landmark-centered condition. The activation was located on the medial surface of the brain, between the occipital and temporal lobes, and included the medial fusiform gyrus, the lingual gyrus, and the posterior part of the parahippocampal gyrus (PH). On the right side, the lingual activation extended more caudally than on the left.

Differential Activation between the Spatial Conditions

Results of direct comparisons between the three spatial conditions are reported in Table 2 and shown in Figure 3. These comparisons were performed in two ways (see Methods for details): voxel by voxel, through standard paired comparisons between conditions (last

Table 2. Differential Activation between the Spatial Conditions

<i>Region</i>	<i>Difference between Conditions in the Mean Regional Signal Increase</i>	<i>Voxel-level Differences</i>
Bilateral parietal–occipital	Landmark-centered > viewer-centered and object-centered	Right middle occipital gyrus ($z = 4.21$) (36, -86, 28) (BA 19) Right ventral precuneus ($z = 4.08$) (24, -62, 20) (BA 23) Right posterior cingulate (retrosplenial) (9, -48, 9) (BA 30) Right anterior calcarine (20, -38, -4) Left superior parietal lobule ($z = 2.91$) (-20, -74, 56) (BA 7) Left middle occipital gyrus ($z = 3.56$) (-36, -82, 32) (BA 19) Left dorsal precuneus ($z = 4.05$) (-8, -74, 60) (BA 7) Left anterior calcarine ($z = 3.55$) (-12, -62, 16) Left posterior cingulate (retrosplenial) ^a ($z = 3.49$) (-4, -46, 20) (BA 30) Left ventral precuneus ^a ($z = 2.96$) (-4, -58, 20) (BA 23)
Right superior frontal	Viewer-centered and Landmark-centered > object-centered	
Right inferior frontal	(no significant differences)	
Left inferior frontal	Viewer-centered > Landmark-centered and object-centered*	
Bilateral lateral occipital–temporal	Object-centered > viewer-centered	
Bilateral medial occipital–temporal	Landmark-centered > viewer-centered and object-centered	Right lingual gyrus (12, -86, -12) (BA 18/19) Right fusiform gyrus ($z = 2.78$) (28, -62, -8) (BA 37) Right parahippocampal gyrus ($z = 4.31$) (32, -38, -12) Left lingual gyrus (-24, -58, -12) (BA 18/19) Left fusiform gyrus ($z = 4.26$) (-28, -50, -8) (BA 37)

Significant differences ($p < .05$) are reported between the mean regional signal increase relative to the control task, computed for each spatial condition in each activated region (middle column). Locations of voxels are also reported, which showed significant differential activation between the conditions when performing voxel-level comparisons (last column). See Table 1 for other details.

^aOutside the regions listed in Table 1.

* $p < .1$.

column in Table 2), and for each region as a whole, by taking each of the regions activated versus the control task and described above, and comparing the mean activation over the region across spatial conditions (middle column in Table 2 and bar graphs in Figure 3).

The parietal-occipital region as a whole was more activated for the landmark-centered than for the viewer-centered [$t(13 \text{ df}) = 3.05, p < .01$] and object-centered [$t(13) = 3.16, p < .01$] conditions. Voxel-level analysis showed that, inside this region, areas showing

increased signal in the landmark-centered condition were located in the left superior parietal cortex (both laterally and medially in the precuneus), in the bilateral middle occipital gyrus, and, on the medial surface of both hemispheres, in the inferior portion of the parietal-occipital sulcus (with the adjacent cuneus/precuneus) and in the anterior calcarine sulcus. Further regions of stronger involvement in the landmark-centered condition relative to the other two conditions were detected in the bilateral posterior cingulate and the ad-

acent ventral precuneus (retrosplenial cortex). Figure 4A shows the location of the retrosplenial activation in individual subjects.

In the frontal lobe, no differences were evident for the right inferior frontal activation, while the right superior frontal cortex was more involved in the viewer-centered [$t(13) = 1.74, p < .05$] and landmark-centered [$t(13) = 2.41, p < .05$] conditions than in the object-centered one. The left inferior frontal cortex showed a tendency to more activation for the viewer-centered

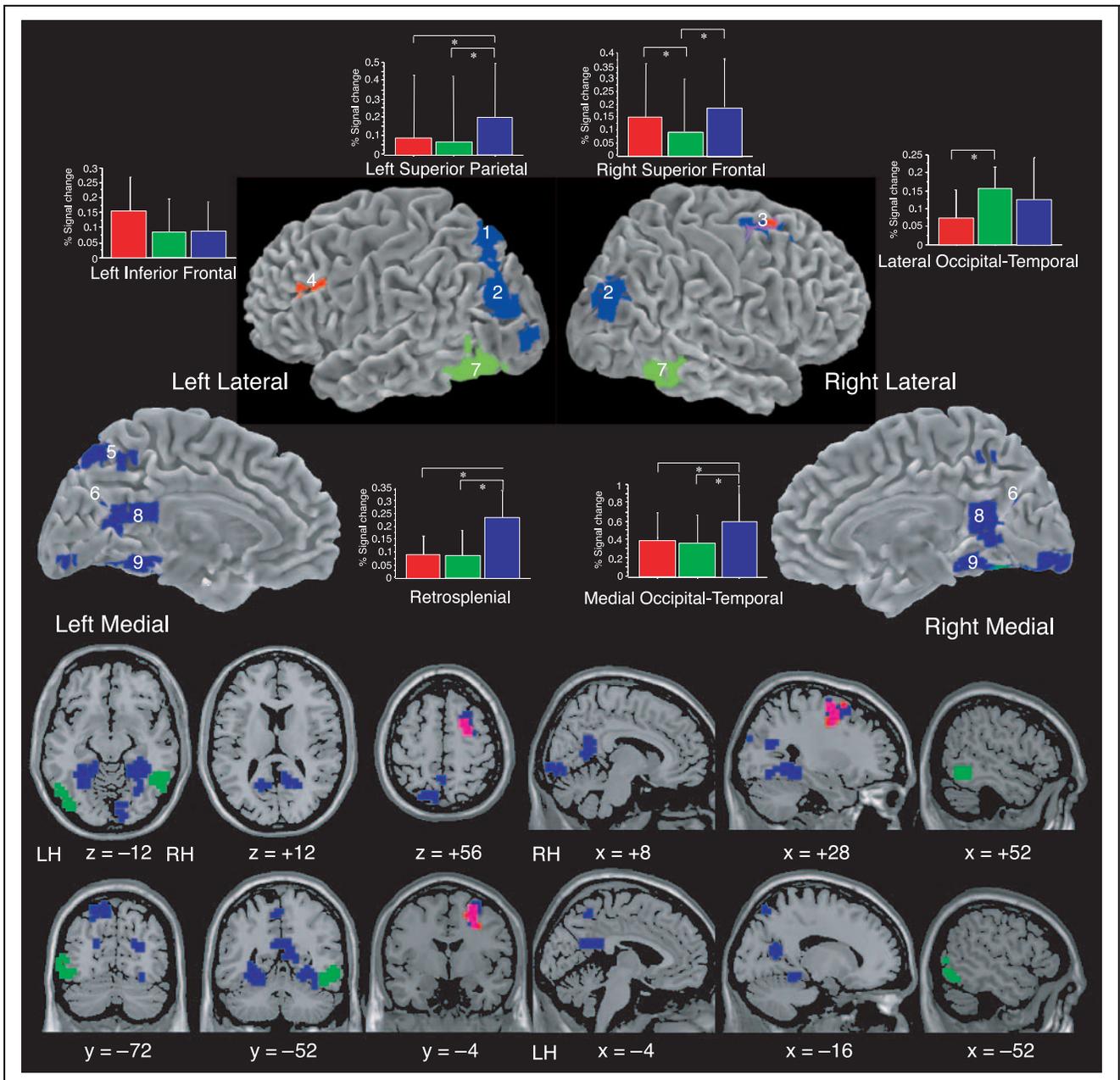


Figure 3. Differential activation between the spatial conditions. Color labels refer to the three spatial conditions as in Figure 2. Lateral and medial three-dimensional views are shown in the upper panel. Bar plots show mean signal increases for each spatial condition relative to the control task in particular regions (see Methods for details). Asterisks denote significantly ($p < .05$) different activation. Selected sagittal, coronal, and transverse slices are shown in the lower panel. Numbers as in Figure 2.

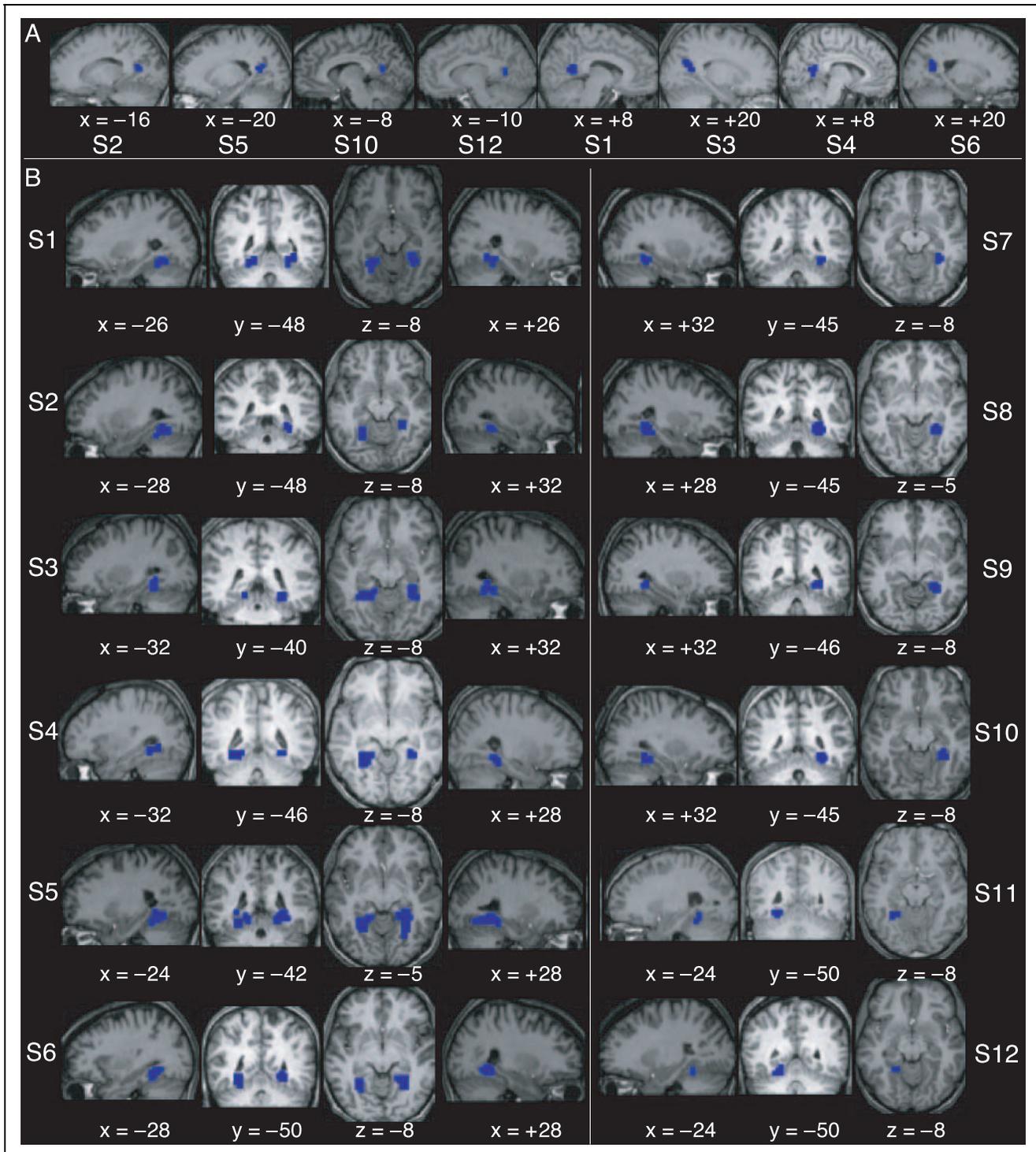


Figure 4. Individual data for the landmark-centered activation. (A) Localization of the medial occipital–parietal and retrosplenial activation in eight subjects. This activation was found bilaterally for two subjects (s5 and s10), on the right for four subjects (s1, s3, s4, s6), and on the left for two subjects (s2, s12). (B) Localization of the ventromedial occipital–temporal activation. This activation was found bilaterally for six subjects (s1–s6), on the right for four subjects (right panel, s7–s10), and on the left for two subjects (s11–s12). Data were analyzed at voxel-level ($p < .01$), restricting the analyses to the brain regions emerged in the group in at least one spatial condition relative to the control.

condition with respect to both the object-centered [$t(13) = 1.47, p = .08$] and the landmark-centered [$t(13) = 1.41, p = .09$] conditions.

The ventrolateral occipital–temporal regions were more activated by the object-centered than by the viewer-centered condition, both in the right [$t(13) =$

2.47, $p < .05$] and in the left [$t(13) = 2.99$, $p < .01$] hemispheres.

Finally, the ventromedial occipital–temporal cortex was more activated in the landmark-centered than in the viewer-centered [$t(13) = 4.16$, $p < .001$] and object-centered [$t(13) = 4.97$, $p < .001$] conditions. Voxel-level analysis showed the same pattern of activation both relative to the viewer-centered and to the object-centered condition, encompassing the right posterior PH and the bilateral fusiform and lingual gyri. Again, the lingual activation extended more caudally on the right. The exploration of individual data showed a strong between-subject consistency as for the anatomical location of this activation, thus making group results well representative (see Figure 4B).

DISCUSSION

Viewer-centered Coding and the Parietal–frontal Cortex

The posterior parietal and frontal premotor network detected during the viewer-centered condition is the same as that found in previous perceptual tasks on egocentric spatial localization (Galati, Committeri, et al., 2001; Galati, Lobel, et al., 2000; Vallar et al., 1999). Although we used real 3-D objects, rather than simple visual stimuli, and a distance judgment task, rather than a left–right position judgment, the results are very congruent. The detected parietal/frontal network is in fact bilateral but more extensive in the right hemisphere, and the center of activity is quite superior and medial. Deficits in visuomotor coordination (e.g., “optic ataxia”) can be observed in humans after dorsal lesions, and both the dorsal precuneus and the superior parietal lobule play a fundamental role in the genesis of such egocentric disorders (Perenin & Vighetto, 1988; Levine, Kaufman, & Mohr, 1978). Accordingly, optic ataxic patients have also a disturbed perception of their body midline (Perenin, 1997), like neglect patients with extensive lesions comprising posterior and superior parietal regions (Hasselback & Butter, 1997).

Unexpectedly, none of the posterior parietal regions revealed a stronger involvement during the egocentric than during the other spatial coding. Galati, Lobel, et al. (2000) had instead detected a clear preference of the posterior parietal cortex for body- versus object-centered tasks. The present viewer-centered condition, which refers to the viewer’s position as a whole rather than to a specific body part (such as the body mid-sagittal plane), may not have fully grasped the body-part-centered nature of egocentric neural coding. In a similar vein, the explicit perceptual judgement may have underestimated the primary action-oriented aspect of egocentric coding, as well as the virtual far space may have underestimated its preference for the near prehension space (Weiss et al., 2000), in both cases reducing the parietal involvement. Alternatively,

viewer-centered and body-centered frames may be intrinsically different.

A region significantly more active for the viewer-centered coding than for the object-centered coding was detected in the frontal lobe. It comprised the so-called deep frontal eye fields (FEFs) (Lobel et al., 2001) and the PMd, respectively coding oculomotor and reaching-related space in egocentric coordinates (e.g., Boussaoud & Bremmer, 1999; Goldberg & Bruce, 1990). The activation included the rostral portion of PMd, recently termed “pre-PMd,” as it is more closely related to cognitive processes than to motor processes (Picard & Strick, 2001). This region receives strong projections from the dorsolateral prefrontal cortex (DLPFC), which has been suggested to play a role in spatial memory (Wilson, Scalaidhe, & Goldman-Rakic, 1993). Interestingly, our activation extended rostrally inside the SFS, in the putative human homologue of DLPFC (Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998). It is worth noting that the whole right superior frontal activation was shared by the viewer-centered and the landmark-centered conditions, suggesting common computational mechanisms.

The left ventral cortex, instead, showed a tendency to prefer the viewer-centered coding. Centered in the left IFG (BAs 44 and 45), it was already detected in previous experiments of body midline perception (Galati, Committeri, et al., 2001; Vallar et al., 1999), during active pointing (e.g., Lacquaniti et al., 1997), and also during passive observation of grasping movements (Rizzolatti, Fadiga, Gallese, & Fogassi, 1996), so that analogies have been drawn with monkey PMv (Rizzolatti, Fogassi, & Gallese, 2002). More specifically, area 44 is considered homologous to the rostral PMv (F5), whereas area 6 to the caudal PMv (F4). PMv is part of those circuits coding peripersonal (F4) and grasping-related space (F5), thus crucially involved in egocentric spatial representations (see Colby, 1998, for a review). Besides the motor role, the present data bring further support to a cognitive role for PMv (Rizzolatti et al., 2002).

Landmark-centered Coding and the Ventromedial Occipital–Temporal Cortex

One of the most interesting new findings of this study is the fact that the bilateral ventromedial occipito-temporal cortex, including the fusiform, lingual, and posterior parahippocampal gyri, was exclusively activated in the landmark-centered condition, where the geometrical structure of the environment had to be taken as a reference. Fusiform, lingual, and parahippocampal gyri have been all associated with the simple passive viewing of buildings/scenes (Haxby et al., 1999; Aguirre, Zarahn, & D’Esposito, 1998; Epstein & Kanwisher, 1998). In the lingual gyrus, this happens in a rostral region (“lingual landmark area” [LLA]) which seems to be crucially involved in the recognition of stimuli with orienting

value. In fact, a lesion here often causes “landmark agnosia” (see Aguirre & D’Esposito, 1999, for a review). On the other hand, a region within the posterior PH (“parahippocampal place area” [PPA]), seems to be implicated more in the encoding of new place information into memory, than in recognition or navigation (Epstein, DeYoe, Press, Rosen, & Kanwisher, 2001; Epstein, Harris, Stanley, & Kanwisher, 1999). Neuroimaging studies repeatedly found a bilateral (Mellet et al., 2000; Aguirre, Detre, et al., 1996; Maguire, Frackowiak, & Frith, 1996) or unilateral right (Maguire, Burgess, et al., 1998; Aguirre & D’Esposito, 1997) PH activation during topographical learning, but also during the recall of recently learned environmental information (Aguirre & D’Esposito, 1997; Ghaem et al., 1997), and when the environment (O’Craven & Kanwisher, 2000) or the landmarks (Ghaem et al., 1997) were only mentally imagined.

Our activation, which encompassed both areas, cannot be due to the simple passive viewing of a building/scene, as stimuli were exactly the same between tasks and conditions, and thus they were subtracted in the various comparisons. The activation cannot even be due to topographical learning, because our subjects had learned the environmental structure before the functional MR session. To perform the task, they had to recall the global environmental geometry from memory, because the central wing of the palace could only be recognized by means of its geometrical relationship with the two lateral wings. Therefore, the ventromedial activation could reflect the coding of the current spatial relationship between the viewer and the environmental geometry (see Epstein, Graham, & Downing, 2003), and its matching with the stored environmental representation. Such behavior recalls the “local-view place cells” (McNaughton, Chen, & Markus, 1991) in the rat hippocampal formation, which fire whenever the animal finds himself in a particular location and with a particular direction. In a similar fashion, the monkey “spatial view cells” respond when the animal looks at a particular part of the environment (Georges-François, Rolls, & Robertson, 1999; Rolls & O’Mara, 1995).

However, an alternate interpretation of the activation of the LLA/PPA cannot be excluded. Attention to buildings has been shown to modulate the activity of the PPA, even in conditions where the presented stimuli included other objects or faces (Avidan, Levy, Hendler, Zohary, & Malach, 2003; O’Craven, Downing, & Kanwisher, 1999; Tong, Nakayama, Vaughan, & Kanwisher, 1998). Thus, in the present study, attention to the building/scene, when it had to be used as reference, may have contributed to the observed activation, by modulating the activity of such specific areas, which do not respond to other kinds of objects (see, for example, Epstein & Kanwisher, 1998). Note however that the differential activation for the landmark-centered

condition extended well beyond the PPA, for example, in the retrosplenial and parietal cortex (see below), where no specificity for buildings has been described. Thus, the attentional interpretation cannot hold for the whole pattern of observed activation.

Our data also suggest that the hippocampus proper in humans is not necessary to judge the position of an object with respect to a landmark or a known environmental geometry. For this reason, they are consistent with the idea that the hippocampus is involved in more complex topographical situations such as, for example, when the environment is made up of different places connected by several possible routes (Burgess, Maguire, & O’Keefe, 2002) or when topographical learning is involved (Hartley et al., 2003; Iaria et al., 2003).

Landmark-centered Coding and the Retrosplenial Cortex

Another region showing a stronger involvement during the landmark-centered condition was the bilateral retrosplenial cortex. The retrosplenial cortex, because of its anatomical interposition between parietal and medial temporal regions and of its strong anatomical links with both areas, has been suggested as the transition zone between egocentric and allocentric/mnemonic representations (e.g., Aguirre & D’Esposito, 1999). Together with visual areas of the ventral system, the superior temporal sulcus and the posterior parietal cortex, the retrosplenial cortex sends inputs to the parahippocampal gyrus and, through it, to the hippocampus (Suzuki & Amaral, 1994a, 1994b).

Previous neuroimaging studies on navigation and orientation in large-scale space consistently detected a bilateral activity in the retrosplenial cortex (Hartley et al., 2003; Mellet et al., 2000; Maguire, Burgess, et al., 1998; Maguire, Frith, et al., 1998; Aguirre & D’Esposito, 1997; Ghaem et al., 1997; Maguire, Frackowiak, & Frith, 1997; Aguirre, Detre, et al., 1996). However, these studies contrasted very different conditions, such as, for example, name–place association and scrambled stimuli (Aguirre & D’Esposito, 1997), not allowing clear conclusions on the specific function of the detected regions. The present experiment, instead, used very specific comparisons: The same distance judgement was performed using the known environmental landmark as a spatial reference, rather than the viewer’s position or a movable object. Therefore, it represents a strong functional evidence of the bilateral retrosplenial specialization for the environmental (landmark-centered) coding of space.

Clinical data suggest that lesions to the right retrosplenial cortex can cause pure topographical disorientation (see Maguire, 2001, for a review), which typically consists in the difficulty of using well-recognized landmarks in order to find the way in familiar environments. Patients are unable to orient themselves and to know

which direction to take, as if they had lost their “heading” within the environment (Aguirre & D’Esposito, 1999). Accordingly, a small population of cells in the retrosplenial cortex of the rat fires only when the rat maintains a certain heading or orientation within the environment (Chen et al., 1994). This behavior was originally discovered in the so-called head-direction cells of the postsubiculum (a region of the dorsal hippocampal formation) (Zugaro, Arleo, Berthoz, & Wiener, 2003; Taube et al., 1990), which constitute the directional input to the hippocampal “place cells” (O’Keefe, Burgess, Donnett, Jeffery, & Maguire, 1999).

In the present paradigm, the sudden change in the point of view which happens from trial to trial may be considered as analogous to disorienting subjects and having them to reorient on the exclusive basis of the visual scene, as no information are available about the occurred displacement. An automatic mechanism of spatial reorientation may well occur in all the spatial conditions, and even in the control task, but we argue that reorientation is much more implicated when information that are used to reorient ourselves, such as the environmental geometry (Wang & Spelke, 2002), have to be explicitly taken into consideration to perform the task. As proposed above, a comparison between the currently perceived environment (local view) and its stored spatial representation, would allow the disoriented subject to determine his position and heading within the environment (Gallistel, 1990).

Landmark-centered Coding and the Parietal Cortex

Significant differences between the spatial conditions have also been detected in dorsal regions, where the bilateral middle occipital gyrus and the left superior parietal cortex (superior parietal lobule and precuneus) appeared to be significantly more active during the landmark-centered than during the other two spatial conditions. Such a lateralization to the left comes from the fact that the landmark-centered condition induced a more symmetrical activity than the viewer- and object-centered conditions (which involved more the right hemisphere).

Together with the retrosplenial cortex, the posterior parietal cortex and the precuneus would participate in the perceptual processing of the visual scene necessary “to establish and maintain one’s bearings” (Hartley et al., 2003). In the monkey, for example, the majority of neurons in parietal area 7a have gain fields for head position that are referenced to the world (the experimental room) (Snyder et al., 1998).

The precuneus seems also to have some relation with memory- and imagery-related processes (Fletcher et al., 1995). In our case, the spatial reference frame used in the landmark-centered condition was part of a stored representation, and was only partially visible. It is rea-

sonable to think that our subjects recalled the stored information and mentally completed the visual scene. Furthermore, the left precuneus has been found more involved during mental navigation in an environment learned from a route perspective, than during spatial tasks on a map learned from a survey perspective (Mellet et al., 2000). To this regard, it is noteworthy that our subjects learned the environment from a route perspective and never saw the map.

As for the middle occipital cortex, it was found to be activated in several previous neuroimaging studies of orientation in large-scale space (e.g., Maguire, Frith, et al., 1998). Moreover, a recent study (Hasson, Harel, Levy, & Malach, 2003) found a dorsal building-specific area located slightly beneath the present cluster of activity. The attentional modulation mechanism put forward in the previous paragraph may accounts for this activation.

Landmark- versus Object-centered Coding

It may be argued that, in the present perceptual paradigm, the presence of an observer and of incoming visual stimulation to be coded by this observer, may have introduced an automatic egocentric component in the other two conditions. Bearing in mind such theoretical argument, the present experiment has been designed for allowing direct comparisons between the different spatial codings and thus revealing regions significantly more involved in each kind of computation.

Landmark- and object-centered coding could simply share the fact of being “not egocentric.” However, the present data show a clear dissociation in activated areas, with the ventromedial occipital-temporal and retrosplenial cortex firmly specialized for the landmark-centered judgements, and the lateral occipital-temporal cortex relatively specialized for the object-centered judgements. Thus, our data indicate that using either a movable object or a stable landmark (i.e., the environmental structure) as a spatial reference involves different brain regions.

It is reasonable to believe that these results represent the neural correlates of a strong dissociation emerged at behavioral level. Recent evidence in rats (Cheng, 1986), monkeys (Gouteux, Thinus-Blanc, & Vauclair, 2001), and human infants and adults (Gouteux & Spelke, 2001; Wang & Spelke, 2000; Hermer & Spelke, 1994), shows that, during spatial reorientation tasks, the surrounding surface geometric layout is handled differently from nongeometric properties of the environment, such as the position or even the geometrical configuration of a set of (potentially movable) objects. Memory for object locations strongly relies on the surrounding surface layout, which solely survives disorientation and allows reorientation (Wang & Spelke, 2000, 2002). The detected ventromedial occipital-temporal and retrosplenial activation during the landmark-centered condi-

tion may represent the neural correlate of such encapsulated module for geometry (Wang & Spelke, 2002).

Even if experimental data are still incongruent, it seems that nongeometric properties can be used in particular situations, as when they are particularly stable or large (Gouteux & Spelke, 2001; Learmonth, Newcombe, & Huttenlocher, 2001). Thus, the activation pattern of the object-centered condition should be more similar to that of the landmark-centered condition if the reference object was stable in the environment and did not change position from trial to trial.

An intriguing result of the present study is the inferior occipital–temporal activation observed for the object-centered coding. It is located more anteriorly than the lateral occipital (LO) region, in which a certain amount of invariance for changes in object position has been described (Grill-Spector et al., 1999). Milner, Jonsrude, and Crane (1997) found a very similar activation during the recall phase of a task that required to memorize the location of objects within two-dimensional arrays. This was observed when the array was shifted with respect to the encoding phase, thus requiring the use of a spatial representation that coded the relationships between objects (as in our object-centered condition). Thus, object-centered coding seems to be implemented also in the ventrolateral object-related cortices, just as the landmark-centered coding is implemented in ventromedial building-specific regions. As pointed above, an attentional bias may also have contributed to the observed activation, by modulating the activity of regions which code objects different from buildings (e.g., Avidan et al., 2003; Wojciulik, Kanwisher, & Driver, 1998).

Previous neuroimaging studies have investigated object-based spatial judgements, such as line bisection (Fink, Marshall, Shah, et al., 2000; Fink, Marshall, Weiss, et al., 2000; Galati et al., 2000; Weiss et al., 2000; Fink, Dolan, et al., 1997). With respect to them, the present object-centered condition activated similar posterior parietal regions, but failed in activating the PMd and early visual processing regions, particularly involved when dealing with far space (Weiss et al., 2000) or when the stimulus is more object-like (Fink, Marshall, Weiss, et al., 2000). Differently from the present experiment, those studies employed judgements relative to the spatial relationships among the component parts of a single object. This may suggest that “within-objects” and “between-objects” spatial coding is treated in different areas in the human brain (Humphreys & Riddoch, 1994). In our case, the important finding is the specificity of the object-centered ventrolateral activation with respect to a viewer-centered spatial coding.

Distance Estimation and the Parietal Lobe

Common parietal activity in the spatial conditions might suggest an eye movements effect. However, eye move-

ments were controlled in the preliminary psychophysical study, thus they cannot have determined the present parietal activation. Even if little can be concluded about a negative result, the most likely interpretation for the parietal involvement is that it has a role in distance computation, that is, a common cognitive component across the three spatial conditions and absent in the control task. Distance estimation is in fact classically disturbed in subjects having lesions to the posterior dorsolateral cortex (e.g., Holmes, 1918; Bálint, 1909).

Conclusions

Object localization in a complex environment requires the conjoint activity of several regions, depending on the spatial reference to be used: if viewer-centered, the parietal lobe and connected frontal premotor regions are recruited, whereas if centered on some external reference, both parietal–frontal and ventral regions play a role. Object-centered spatial judgements involve the ventrolateral occipital–temporal cortex, while landmark-centered judgements require a strongly specialized circuit of ventromedial occipital–temporal and retrosplenial regions. In our opinion, this circuit mainly reflects the matching between the stored environmental representation and the currently perceived environmental layout. Interestingly, it may represent the neural correlate of the encapsulated module for spatial reorientation based on environmental geometry. Finally, the parietal cortex (except for the left superior parietal lobule and precuneus, which have a preference for the landmark-centered condition) seems to play a general role in spatial distance estimation, together with the right PMv.

METHODS

Participants

Fourteen neurologically normal volunteers (7 women and 7 men, mean age 26, range 23–33) gave their informed consent to participate in the experiment, whose procedures had received local ethical approval. Twelve subjects were right-handed and two were left-handed, as assessed by a modified version of the Edinburgh Inventory (Oldfield, 1971) (mean index = + 0.7; *SD* 0.5).

The Virtual Environment

A virtual reality software (3DStudio Max 4.2, Autodesk, Discreet) was used to create a three-dimensional realistic reconstruction of a complex environment, representing a square arena in front of the entrance of a palace. The arena is defined by the two short lateral wings and the long central wing of the palace. The remaining side is open and occupied by a lawn. The square has no

fixed furnishings, except for a fountain and four benches. The central frame in Figure 1 shows an aerial view of the environment.

Stimuli

During the experiment, the participants were shown a different snapshot (of about $18^\circ \times 14^\circ$ of visual angle) of the environment in each trial. Each snapshot simulated a photograph of the environment taken from 1 of 12 different points of view. The only constraint was that at least part of the long central wing of the palace was always visible. The small frames in Figure 1 show the chosen camera positions and the corresponding snapshots.

In each snapshot, three different objects were also visible: one reference object (a red ball), and two target objects (a big green and a small blue garbage can: see examples in Figure 1). These three objects occupied a different position in each trial. In other words, we could imagine that, between trials, the observer and the three objects had independently moved to different locations in the environment. Moreover, one of the two garbage cans was laying on the ground in each snapshot.

Images were carefully built in order to allow an easy identification of the objects (always showed in their canonical perspective). The long central wing of the palace was always very easy to distinguish, because of its evident geometrical relationships with the two lateral wings and the fountain. Furthermore, we balanced the spatial location of the different objects across trials with respect to the point of view (i.e., their position on the screen). We used four different images for each of the 12 possible points of view, for a total of 48 stimuli. Among these, eight combinations of response (green or blue) and frame of reference (viewer-centered, object-centered, and landmark-centered) were possible, so that six different images were used for each combination. The same 48 stimuli were employed for each of the four conditions (three spatial and one non-spatial).

A preliminary psychophysical study was performed on a separate group of eight subjects in order to match difficulty, in terms of errors and mean reaction times, across the spatial conditions. To this aim, we tried different absolute and relative distances of the two target objects from the three possible spatial references. Matching real distances across conditions (i.e., having the two target objects at the same distance from each of the three spatial references in each snapshot) resulted in different reaction times, so we chose not to balance either absolute or relative distances, but rather to select distances which gave similar reaction times across conditions. In the same psychophysical study, we also controlled for total number of eye movements through a video camera. We found no differences between the three spatial conditions, and also between each of them and the control task (mean saccades per trial: 2.1).

Cognitive Tasks

Participants were given two response buttons, associated with the green and the blue garbage cans, respectively. The experimental task required to judge which of the two garbage cans was closer to a particular spatial reference. In the “viewer-centered condition,” participants were instructed to respond as quickly as possible by pressing the button corresponding to the garbage can that was closer to their current position (i.e., to the current point of view). This condition requires a distance judgment with respect to the current observer’s position. Because the point of view and both the viewer-relative and the absolute position of the two garbage cans vary from trial to trial, the position of the viewer and of the objects in the environment is completely irrelevant. In the “object-centered condition,” participants were instructed to respond as quickly as possible by pressing the button corresponding to the garbage can that was closer to the reference object (the red ball). This condition requires a distance judgment with respect to an object, whereas the observer’s position is completely irrelevant. Note that the position of the reference object in the environment changes at every trial, therefore the reference object cannot be considered as a landmark and participants cannot use any information about the spatial features of the environment to solve the task. That is to say, this condition requires only a between-objects frame, not involving environmental representations. In the “landmark-centered condition,” participants were instructed to respond as quickly as possible by pressing the button corresponding to the garbage can that was closer to the central wing of the palace. This condition requires to refer to an enduring geometrical feature of the environment, rather than to a specific object that moves each time. Crucially, this condition requires to access a mental reconstruction of the overall environmental geometry: The central wing has to be recognized by means of its geometrical relationships with the lateral wings. Finally, in the “control task,” participants were instructed to respond as quickly as possible by pressing the button corresponding to the garbage can that was lying on the ground. This task does not require to estimate position and distance, but still requires to shift attention to the target objects, to identify them and to press one of the response buttons accordingly.

Apparatus

Imaging was performed on a General Electric Signa 1.5-T whole-body scanner, equipped for echo-planar imaging. All images were acquired using a standard quadrature head coil. Head movement was minimized by mild restraint and cushioning. Stimuli were generated by a PC located outside the MR room, which ran the Presenta-

tion 0.43 software (www.neurobehavioralsystems.com). Stimuli were projected on a back projection screen using an LCD video projector. Participants viewed the stimuli through mirror glasses. Responses were given by using two locally fabricated push-buttons connected to the control computer.

Procedure

Prior to MR imaging, participants underwent a preliminary training session. First, they were shown a 1-min animation on a computer screen simulating a rapid circular walking in the environment, in order to familiarize with it. Then the same animation was shown again, this time with the three objects present in the environment and repeated several times in several different positions, in order to familiarize subjects with object aspect and size. Then, a single aerial view of the environment was shown, followed by a series of images representing the 12 possible camera points of view used in the experiment. Participants were then instructed about tasks, and started a 2 min 24 sec training session in which a reduced set of the experimental stimuli was employed, with a presenting rate (1500 msec) slightly slower than the imaging experiment, in order to allow a first approach to the response procedure. A second training session was performed with the same timing as the imaging experiment and repeated once or twice, depending on the level of accuracy reached by the subject.

Each participant underwent one functional MR imaging acquisition run, while we acquired 195 consecutive volumes. The first three volumes were discarded to achieve steady-state T1-weighting, and the experiment started at the beginning of the fourth volume. The experiment consisted in 32 blocks (eight per condition) lasting 18 sec each. Two sequences of stimuli and blocks were created by randomly placing blocks within the run and randomly placing stimuli within each block, the only constraints being a maximum distance of 1 min 30 sec between two blocks of the same task or condition, and no more than two consecutive blocks of the same task or condition. Each participant was randomly assigned to one of the two sequences.

At the beginning of each block, an instruction about the task and condition to perform during the incoming block appeared in the middle of the screen for 1.5 sec, followed by a 0.4° fixation cross for 1.5 sec. A series of six 2.5-sec trials followed. In each trial, a snapshot of the environment appeared for 1 sec, followed by the 1.5-sec fixation cross. Such a fast presentation rate was chosen in order to minimize eye movements.

Imaging Parameters

Echo-planar functional MR images (TR = 3 sec, TE = 60 msec, flip angle = 90°, image matrix = 64 × 64,

FOV = 240 × 240 mm, voxel size = 3.75 × 3.75 × 4 mm) were acquired in the axial plane using blood oxygenation level-dependent (BOLD) imaging (Kwong, Belliveau, & Chesler, 1992). Twenty-nine transverse slices were acquired without gaps. From the superior convexity, sampling included almost all the cerebral cortex, excluding only the ventral portion of the cerebellum. A three-dimensional high-resolution anatomical image was also acquired for each subject (124 sagittal slices, TR = 10 msec, TE = 2.2 msec, TI = 600 msec, flip angle = 10°, image matrix = 256 × 192, FOV = 240 × 180 mm, voxel size = 0.94 × 0.94 × 1.2 mm).

Image Processing and Analysis

Image preprocessing and statistical analysis were performed using the SPM99 software platform (Wellcome Department of Cognitive Neurology, London, UK), implemented in MATLAB (The MathWorks, Natick, MA, USA).

Head movements occurring between functional scans were calculated and a motion correction was applied when movement exceeded either 1° of rotation or 1 mm of translation. Functional MR images were then transformed into a standard space, using transformation parameters determined from the anatomical image through an automatic nonlinear stereotaxic normalization procedure (Friston et al., 1995). The template image was based on average data provided by the Montreal Neurological Institute (MNI brain: Mazziotta, Toga, Evans, Fox, & Lancaster, 1995) and conformed to a standard coordinate referencing system (Talairach & Tournoux, 1988). The final voxel size after normalization was an isotropic 4 mm. Functional images were then spatially smoothed using an isotropic gaussian kernel (8 mm full-width-at-half-maximum).

Group analysis was performed using a two-stage random-effect approach (Friston, Holmes, & Worsley, 1999; Holmes & Friston, 1998). At the first stage, the time series of functional MR images obtained from each participant was analyzed separately. The effects of the experimental paradigm were estimated on a voxel-by-voxel basis, according to the general linear model (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994; Worsley, Evans, Marret, & Neelin, 1992). The experimental blocks were modeled as box-car functions, convolved with a synthetic hemodynamic response function. Subject-specific contrast images were then entered at the second stage into one-sample *t* tests, testing the null hypothesis that the mean effect size was equal to zero in the whole population from which our participants were extracted. For each effect of interest, we obtained a statistical parametric map of the *t* statistic. Clusters of adjacent voxels surviving a threshold of $p < .01$ were formed and characterized in terms of

spatial extent. The significance of each cluster was estimated using distribution approximations from the theory of gaussian fields (Worsley, Marret, Neelin, Friston, & Evans, 1995; Worsley, Evans, et al., 1992), resulting in a corrected p value. Correction was applied over the whole brain, or in some cases, over a more limited search volume (see below). Activation clusters were retained as significant at $p < .05$ corrected.

First, we inspected activation for each kind of spatial judgment with respect to the control task (Table 1). Then, we explored differential activation between the spatial conditions using two approaches (Table 2): (a) We performed pairwise voxel-level comparisons between the three spatial conditions, using p value correction over the set of voxels emerged as activated in at least one spatial condition relative to control. Also regions outside this limited volume are reported, when reaching a significant p value corrected over the whole brain; (b) We computed the mean signal increase for each spatial condition relative to the control task over each activated cluster and performed paired t tests on these data. Differences were retained as significant at $p < .05$. This kind of approach has less localizing power than the voxel-based approach, but offers more sensitivity when the spatial resolution of the signal is lower than voxel size (Friston, Holmes, Poline, Price, & Frith, 1996). Mean signal increases over a given cluster were computed in terms of the first eigenvariate of the BOLD response amplitudes estimated at the first analysis stage (i.e., in each subject) in all voxels of the cluster.

Localization and visualization of activations were achieved by using the in-house BrainShow software, which allows to superimpose statistical maps on brain slices and on folded, inflated, and flattened representations of the cortical surface. For visualization of group activations, we used the cortical surface of the single-subject MNI brain, reconstructed using the FreeSurfer software (surfer.nmr.mgh.harvard.edu). Anatomical labels were automatically assigned to activated areas by the BrainShow software, based on a macroscopical anatomical parcellation of the MNI single-subject brain (Tzourio-Mazoyer et al., 2002), and then manually checked with reference to a standard atlas (Duvernoy, 1991).

Acknowledgments

We thank the UNAF/SHFJ/CEA and IFR44, Manuel Vidal and Nicholas Nebiolo for their help in building the 3-D environment, and Jean-Baptiste Poline for his methodological advice. This research was funded by Italian Ministry of Health and European Laboratory of Neurophysiology and Neuropsychology of Action (LENNA).

Reprint requests should be sent to Giorgia Committeri, Laboratorio di Neuroimmagini, Fondazione Santa Lucia, via Ardeatina 306, 00179 Rome, Italy, or via e-mail: giorgia.committeri@uniroma1.it.

The data reported in this experiment have been deposited on the fMRI Data Center (<http://www.fmridc.org>). The accession number is 2-2004-116 KQ.

REFERENCES

- Aguirre, G. K., & D'Esposito, M. (1997). Environmental knowledge is subserved by separable dorsal/ventral neural areas. *Journal of Neuroscience*, *17*, 2512–2518.
- Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: A synthesis and taxonomy. *Brain*, *122*, 1613–1628.
- Aguirre, G. K., Detre, J. A., Alsup, D. C., & D'Esposito, M. (1996). The parahippocampus subserves topographical learning in man. *Cerebral Cortex*, *6*, 823–829.
- Aguirre, G. K., Zarahn, E., & D'Esposito, M. (1998). An area within human ventral cortex sensitive to “building” stimuli: Evidence and implications. *Neuron*, *21*, 373–383.
- Avidan, G., Levy, I., Hendler, T., Zohary, E., & Malach, R. (2003). Spatial vs. object specific attention in high-order visual areas. *Neuroimage*, *19*, 308–318.
- Bálint, A. (1909). Seelenlahmung des Schauens, optische ataxie, raumliche storung der aufmerksamkeit. *Monatsschrift für Psychiatrie und Neurologie*, *25*, 51–81.
- Berthoz, A. (1997). Parietal and hippocampal contribution to topokinetic and topographic memory. *Philosophical Transactions of the Royal Society of London, Series B*, *352*, 1437–1448.
- Bisiach, E. (1997). The spatial features of unilateral neglect. In P. Thier & H.-O. Karnath (Eds.), *Parietal lobe contributions to orientation in 3D space* (pp. 465–495). Heidelberg: Springer-Verlag.
- Boussaoud, D., & Bremmer, F. (1999). Gaze effects in the cerebral cortex: Reference frames for space coding and action. *Experimental Brain Research*, *128*, 170–180.
- Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron*, *35*, 625–641.
- Chen, L. L., Lin, L.-H., Green, E. J., Barnes, C. A., & McNaughton, B. L. (1994). Head-direction cells in the rat posterior cortex: I. Anatomical distribution and behavioral modulation. *Experimental Brain Research*, *101*, 8–23.
- Cheng, K. (1986). A purely geometric module in the rat's spatial representation. *Cognition*, *23*, 149–178.
- Cohen, Y. E., & Andersen, R. A. (2002). A common reference frame for movement plans in the posterior parietal cortex. *Nature Review Neuroscience*, *3*, 553–562.
- Colby, C. L. (1998). Action-oriented spatial reference frames in cortex. *Neuron*, *20*, 15–24.
- Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science*, *279*, 1347–1351.
- Driver, J. (1999). Egocentric and object-based visual neglect. In *Spatial functions of the hippocampal formation and the parietal cortex* (pp. 67–89). Oxford: Oxford University Press.
- Duvernoy, H. (1991). *The human brain. Surface, tri-dimensional sectional anatomy and MRI*. Wien: Springer-Verlag.
- Epstein, R., DeYoe, E. A., Press, D. Z., Rosen, A. C., & Kanwisher, N. (2001). Neuropsychological evidence for a topographical learning mechanism in parahippocampal cortex. *Cognitive Neuropsychology*, *18*, 481–508.
- Epstein, R., Graham, K. S., & Downing, P. E. (2003). Viewpoint-specific representations in human parahippocampal cortex. *Neuron*, *37*, 865–876.

- Epstein, R., Harris, A., Stanley, D., & Kanwisher, N. (1999). The parahippocampal place area: Recognition, navigation, or encoding? *Neuron*, *23*, 115–125.
- Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, *392*, 598–601.
- Fink, G. R., Dolan, R. J., Halligan, P. W., Marshall, J. C., & Frith, C. D. (1997). Space-based and object-based visual attention: shared and specific neural domains. *Brain*, *120*, 2013–2028.
- Fink, G. R., Marshall, J. C., Shah, N. J., Weiss, P. H., Halligan, P. W., Grosse-Ruyken, M., Ziemons, K., Zilles, K., & Freund, H. J. (2000). Line bisection judgements implicate right parietal cortex and cerebellum as assessed by fMRI. *Neurology*, *54*, 1324–1331.
- Fink, G. R., Marshall, J. C., Weiss, P. H., Shah, N. J., Toni, I., Halligan, P. W., & Zilles, K. (2000). “Where” depends on “what”: A differential functional anatomy for position discrimination in one- versus two-dimensions. *Neuropsychologia*, *38*, 1741–1748.
- Fletcher, P. C., Frith, C. D., Baker, S. C., Shallice, T., Frackowiak, R. S. J., and Dolan, R. J. (1995). The mind’s eye—Precuneus activation in memory-related imagery. *Neuroimage*, *2*, 195–200.
- Friston, K. J., Ashburner, J., Poline, J. B., Frith, C. D., Heather, J. D., & Frackowiak, R. S. J. (1995). Spatial registration and normalization of images. *Human Brain Mapping*, *2*, 165–189.
- Friston, K. J., Holmes, A. P., & Worsley, K. J. (1999). How many subjects constitute a study? *Neuroimage*, *10*, 1–5.
- Friston, K. J., Holmes, A., Poline, J. B., Price, C. J., & Frith, C. D. (1996). Detecting activations in PET and fMRI: levels of inference and power. *Neuroimage*, *4*, 223–235.
- Friston, K. J., Worsley, K. J., Frackowiak, R. S. J., Mazziotta, J. C., & Evans, A. C. (1994). Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping*, *1*, 214–220.
- Galati, G., Committeri, G., Sanes, J. N., & Pizzamiglio, L. (2001). Spatial coding of visual and somatic sensory information in body-centered coordinates. *European Journal of Neuroscience*, *14*, 737–746.
- Galati, G., Lobel, E., Berthoz, A., Pizzamiglio, L., Le Bihan, D., & Vallar, G. (2000). The neural basis of egocentric and allocentric coding of space in humans: A functional magnetic resonance study. *Experimental Brain Research*, *133*, 156–164.
- Gallistel, C. R. (1990). *The organization of learning*. Cambridge: MIT Press.
- Georges-François, P., Rolls, E. T., & Robertson, R. G. (1999). Spatial view cells in the primate hippocampus: Allocentric view not head direction or eye position or place. *Cerebral Cortex*, *9*, 197–212.
- Ghaem, O., Mellet, E., Crivello, F., Tzourio, N., Mazoyer, B., Berthoz, A., & Denis, M. (1997). Mental navigation along memorized routes activates the hippocampus, precuneus and insula. *NeuroReport*, *8*, 739–744.
- Goldberg, M. E., & Bruce, C. J. (1990). Primate frontal eye fields: III. Maintenance of a spatially accurate saccade signal. *Journal of Neurophysiology*, *64*, 489–508.
- Gouteux, S., & Spelke, E. S. (2001). Children’s use of geometry and landmarks to reorient in an open space. *Cognition*, *81*, 119–148.
- Gouteux, S., Thinus-Blanc, C., & Vauclair, J. (2001). Rhesus monkey use of geometric and nongeometric information during a reorientation task. *Journal of Experimental Psychology: General*, *130*, 505–519.
- Gron, G., Wunderlich, A. P., Spitzer, M., Tomczak, R., & Riepe, M. W. (2000). Brain activation during human navigation: Gender-different neural networks as substrate of performance. *Nature Neuroscience*, *3*, 404–408.
- Grill-Spector, K., Kushnir, T., Edelman, S., Avidan, G., Itzhak, Y., & Malach, R. (1999). Differential processing of objects under various viewing conditions in the human lateral occipital complex. *Neuron*, *24*, 187–203.
- Habib, M., & Sirigu, A. (1987). Pure topographical disorientation: A definition and anatomical basis. *Cortex*, *23*, 73–85.
- Hartley, T., Maguire, E. A., Spiers, H. J., & Burgess, N. (2003). The well-worn route and the path less traveled: Distinct neural bases of route following and wayfinding in humans. *Neuron*, *37*, 877–888.
- Hasselback, M., & Butter, C. M. (1997). Ipsilesional displacement of egocentric midline in neglect patients with, but not in those without, extensive parietal damage. In P. Theier & H.-O. Karnath (Eds.), *Parietal lobe contributions to orientation in 3D space* (pp. 579–595). Heidelberg: Springer-Verlag.
- Hasson, U., Harel, M., Levy, I., & Malach, R. (2003). Large-scale mirror-symmetry organization of human occipito-temporal object areas. *Neuron*, *37*, 1027–1041.
- Haxby, J. V., Ungerleider, L. G., Clark, V. P., Schouten, J. L., Hoffman, E. A., & Martin, A. (1999). The effect of face inversion on activity in human neural system for face and object perception. *Neuron*, *22*, 189–199.
- Hermer, L., & Spelke, E. (1994). A geometric process for spatial reorientation in young children. *Nature*, *370*, 57–59.
- Holmes, A. P., & Friston, K. J. (1998). Generalizability, random effects, and population inference. *Neuroimage*, *7*, S754.
- Holmes, G. (1918). Disturbances of visual orientation. *British Journal of Ophthalmology*, *2*, 443–468, 506–516.
- Honda, M., Wise, S. P., Weeks, R. A., Deiber, M.-P., & Hallett, M. (1998). Cortical areas with enhanced activation during object-centred spatial information processing. *Brain*, *121*, 2145–2158.
- Howard, I. P. (1982). *Human visual orientation*. Chichester: Wiley.
- Humphreys, G. W., & Riddoch, M. J. (1994). Attention to within-object and between-object spatial representations. Multiple sites for visual selection. *Cognitive Neuropsychology*, *11*, 207–241.
- Iaria, G., Petrides, M., Dagher, A., Pike, B., & Bohbot, V. (2003). Cognitive strategies dependent on hippocampus and caudate nucleus in human navigation: Variability and change with practice. *Journal of Neuroscience*, *23*, 5945–5952.
- Kwong, K. K., Belliveau, J. W., & Chesler, D. A. (1992). Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proceedings of the National Academy of Sciences, U.S.A.*, *89*, 5675–5679.
- Jeannerod, M., & Biguer, B. (1989). Référence égoцентриque et espace représenté. *Revue Neurologique*, *145*, 635–639.
- Lacquaniti, F., Perani, D., Guigon, E., Bettinardi, V., Carrozzo, M., Grassi, F., Rossetti, Y., & Fazio, F. (1997). Visuomotor transformations for reaching to memorized targets: A PET study. *Neuroimage*, *5*, 129–146.
- Learmonth, A. E., Newcombe, N. S., & Huttenlocher, J. (2001). Toddler’s use of metric information and landmarks to reorient. *Journal of Experimental Child Psychology*, *80*, 225–244.
- Levine, D. N., Kaufman, K. J., & Mohr, J. P. (1978). Inaccurate reaching associated with a superior parietal lobe tumor. *Neurology*, *28*, 556–561.
- Lobel, E., Kahane, P., Leonards, U., Grosbras, M. H., Lehericy, S., LeBihan, D., & Berthoz, A. (2001). Localization of human frontal eye fields: Anatomical and functional findings of

- functional magnetic resonance imaging and intracerebral electrical stimulation. *Journal of Neurosurgery*, *95*, 804–815.
- Maguire, E. A. (2001). The retrosplenial contribution to human navigation: A review of lesion and neuroimaging findings. *Scandinavian Journal of Psychology*, *42*, 225–238.
- Maguire, E. A., Burgess, N., Donnett, J. G., Frackowiak, R. S. J., Frith, C. D., & O'Keefe, J. (1998). Knowing where and getting there: A human navigation network. *Science*, *280*, 921–924.
- Maguire, E. A., Frackowiak, R. S. J., & Frith, C. D. (1996). Learning to find your way: a role for the human hippocampal formation. *Proceedings of the Royal Society of London, Series B. Biological Sciences*, *263*, 1745–1750.
- Maguire, E. A., Frackowiak, R. S. J., & Frith, C. D. (1997). Recalling routes around London: Activation of the right hippocampus in taxi drivers. *Journal of Neuroscience*, *17*, 7103–7110.
- Maguire, E. A., Frith, C. D., Burgess, N., Donnett, J. G., & O'Keefe, J. (1998). Knowing where things are: Parahippocampal involvement in encoding object locations in virtual large-scale space. *Journal of Cognitive Neuroscience*, *10*, 61–76.
- McNaughton, B. L., Chen, L. & Markus, E. J. (1991). "Dead reckoning", landmark learning, and the sense of direction: A neurophysiological and computational hypothesis. *Journal of Cognitive Neuroscience*, *3*, 190–202.
- McNaughton, B. L., Leonard, B., & Chen, L. (1989). Cortical-hippocampal interactions and cognitive mapping: A hypothesis based on reintegration of the parietal and inferotemporal pathways for visual processing. *Psychobiology*, *17*, 230–235.
- Mazziotta, J. C., Toga, A. W., Evans, A., Fox, P., & Lancaster, J. (1995). A probabilistic atlas of the human brain: Theory and rationale for its development. The International Consortium for Brain Mapping (ICBM). *Neuroimage*, *2*, 89–101.
- Mellet, E., Briscogne, S., Tzourio-Mazoyer, N., Ghaem, O., Petit, L., Zago, L., Etard, O., Berthoz, A., Mazoyer, B., & Denis, M. (2000). Neural correlates of topographic mental exploration: The impact of route versus survey perspective learning. *Neuroimage*, *12*, 588–600.
- Milner, B., Johnsrude, I., & Crane, J. (1997). Right medial temporal-lobe contribution to object-location memory. *Philosophical Transactions of the Royal Society of London, Series B*, *352*, 1469–1574.
- O'Craven, K. M., Downing, P. E., & Kanwisher, N. (1999). fMRI evidence for objects as the units of attentional selection. *Nature*, *401*, 584–587.
- O'Craven, K. M., & Kanwisher, N. (2000). Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *Journal of Cognitive Neuroscience*, *12*, 1013–1023.
- O'Keefe, J., Burgess, N., Donnett, J. G., Jeffery, K. J., & Maguire, E. A. (1999). Place cells, navigational accuracy, and the human hippocampus. *Philosophical Transactions of the Royal Society of London, Series B*, *353*, 1333–1340.
- O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as spatial map. Preliminary evidence from unit activity in the freely moving rat. *Brain Research*, *34*, 171–175.
- O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, *9*, 97–113.
- Olson, C. R., & Gettner, S. N. (1995). Object-centered direction selectivity in the macaque supplementary eye field. *Science*, *269*, 985–988.
- Ono, T., Nakamura, K., Nishijo, H., & Eifuku, S. (1993). Monkey hippocampal neurons related to spatial and nonspatial functions. *Journal of Neurophysiology*, *70*, 1516–1529.
- Perenin, M. T. (1997). Optic ataxia and unilateral neglect: Clinical evidence for dissociable spatial functions in posterior parietal cortex. In P. Thier & H.-O. Karnath (Eds.), *Parietal lobe contributions to orientation in 3D space* (pp. 289–308). Heidelberg: Springer-Verlag.
- Perenin, M. T., & Vighetto, A. (1988). Optic ataxia: Specific disruption in visuomotor mechanisms. *Brain*, *111*, 643–674.
- Picard, N., & Strick, P. L. (2001). Imaging the premotor areas. *Current Opinion in Neurobiology*, *11*, 663–672.
- Pizzamiglio, L., Committeri, G., Galati, G., & Patria, F. (2000). Psychophysical properties of line bisection and body midline perception in unilateral neglect. *Cortex*, *36*, 469–484.
- Rizzolatti, G., Fadiga, L., Gallese, V., & Fogassi, L. (1996). Premotor cortex and the recognition of motor action. *Brain*, *119*, 593–609.
- Rizzolatti, G., Fogassi, L., & Gallese, V. (2002). Motor and cognitive functions of the ventral premotor cortex. *Current Opinion in Neurobiology*, *12*, 149–154.
- Rolls, E. T., & O'Mara, S. M. (1995). View-responsive neurons in the primate hippocampal complex. *Hippocampus*, *5*, 409–424.
- Snyder, L. H., Grieve, K. L., Brotchie, P., and Andersen, R. (1998). Separate body- and world-referenced representations of visual space in parietal cortex. *Nature*, *394*, 887–891.
- Spiers, H. J., Burgess, N., Hartley, T., Vargha-Khadem, F., & O'Keefe, J. (2001). Bilateral hippocampal pathology impairs topographical and episodic but not recognition memory. *Hippocampus*, *11*, 715–725.
- Suzuki, W. A., & Amaral, D. G. (1994a). Perirhinal and parahippocampal cortices of the macaque monkey: Cortical afferents. *Journal of Comparative Neurology*, *350*, 497–533.
- Suzuki, W. A., & Amaral, D. G. (1994b). Topographic organization of the reciprocal connections between the monkey entorhinal cortex and the perirhinal and parahippocampal cortices. *Journal of Neuroscience*, *14*, 1856–1877.
- Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.
- Taube, J. S., Muller, R. U., & Ranck, J. B. (1990). Head-direction cells recorded from the postsubiculum in freely-moving rats: I. Description and quantitative analysis. *Journal of Neuroscience*, *15*, 173–189.
- Tong, F., Nakayama, K., Vaughan, J. T., & Kanwisher, N. (1998). Binocular rivalry and visual awareness in human extrastriate cortex. *Neuron*, *21*, 753–759.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., & Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage*, *15*, 273–289.
- Vallar, G. (1998). Spatial hemineglect in humans. *Trends in Cognitive Sciences*, *2*, 87–97.
- Vallar, G., Guariglia, C., & Rusconi, M. L. (1997). Modulation of the neglect syndrome by sensory stimulation. In P. Thier & H.-O. Karnath (Eds.), *Parietal lobe contributions to orientation in 3D space* (pp. 555–578). Heidelberg: Springer-Verlag.
- Vallar, G., Lobel, E., Galati, G., Berthoz, A., Pizzamiglio, L., & Le Bihan, D. (1999). A fronto-parietal system for computing the egocentric spatial frame of reference in humans. *Experimental Brain Research*, *124*, 281–286.

- Wang, R. F., & Spelke, E. S. (2000). Updating egocentric representations in human navigation. *Cognition*, *77*, 215–250.
- Wang, R. F., & Spelke, E. S. (2002). Human spatial representation: Insights from animals. *Trends in Cognitive Sciences*, *6*, 376–382.
- Weiss, P. H., Marshall, J. C., Wunderlich, G., Tellmann, L., Halligan, P. W., Freund, H.-J., Zilles, K., & Fink, G. R. (2000). Neural consequences of acting in near versus far space: A physiological basis for clinical dissociations. *Brain*, *123*, 2531–2541.
- Wilson, F. A., Scaldie, S. P., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science*, *260*, 1955–1958.
- Wojciulik, E., Kanwisher, N., & Driver, J. (1998). Covert visual attention modulates face-specificity in the human fusiform gyrus: fMRI study. *Journal of Neurophysiology*, *79*, 1574–1578.
- Worsley, K. J., Evans, A. C., Marrett, S., & Neelin, P. (1992). A three-dimensional statistical analysis for rCBF activation studies in human brain. *Journal of Cerebral Blood Flow and Metabolism*, *12*, 900–918.
- Worsley, K. J., Marret, S., Neelin, P., Friston, K. J., Evans, A. (1995). *A unified statistical approach for determining significant signals in images of cerebral activation*. San Diego: Academic Press.
- Zugaro, M. B., Arleo, A., Berthoz, A., & Wiener, S. I. (2003). Rapid spatial reorientation and head direction cells. *Journal of Neuroscience*, *23*, 3478–3482.