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Mental navigation along memorized routes activates the hippocampus, precuneus, and insula

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POSITRON emission tomography was used to investigate the functional anatomy of mental simulation of routes (MSR) in five normal volunteers. Normalized regional cerebral blood flow was measured while subjects mentally navigated between landmarks of a route which had been previously learned by actual navigation. This task was contrasted with both static visual imagery of landmarks (VIL) and silent Rest. MSR appears to be subserved by two distinct networks: a non-specific memory network including the posterior and middle parts of the hippocampal regions, the dorsolateral prefrontal cortex and the posterior cingulum, and a specific mental navigation network, comprising the left precuneus, insula and medial part of the hippocampal regions.

Key words: Cerebral blood flow; Hippocampus; Insula; Memory; Mental imagery; Navigation; PET; Precuneus

Introduction

Locomotion planning requires two essential mental procedures: the construction of internal spatial representations and their reactivation by memory. For cognitive psychology, spatial representations may be encoded and retrieved from two distinct perspectives.[1–3] The survey perspective refers to a bird's eye view, information about landmark being available in an allocentric frame of reference of cardinal points. The route perspective refers to procedural knowledge acquired from navigation with sequential recording of spatial information in an egocentric frame of reference[4], actual navigation being the most common way of building internal representations of this kind. The neurobiological bases of spatial navigation memory in animals have been extensively investigated,[5–7] in particular the role played by the hippocampal formation. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) have been used recently to study navigation encoding in humans,[8,9] and have demonstrated the involvement of parahippocampal gyri in this process. By contrast, very few neuroimaging studies have dealt with the recall of memorized routes. Mental simulation of routes implies the recollection of information linked to one's own experience composed of complex sensory and kinaesthetic sequences, which can be achieved through mental images in a format structurally similar to that of perceptual envents. There is some evidence that motor imagery and movement execution share common cerebral structures,[10,11] as is also the case for visual imagery and visual perception.[12,13] In the present study, we used PET to assess the cerebral structures involved in the mental simulation of routes memorized from previous actual navigation, testing the hypothesis that such a complex mental imagery task shares common brain regions with navigation encoding.

Subjects and Methods

Subjects: Five healthy right-handed young male volunteers (aged 20–22 years) participated in the study. They were selected among a population of 80 medical school students according to their high scores on two visuo-spatial mental ability tests: the Minnesota Paper Form Board (MPFB)[14] and the Mental Rotations Test (MRT).[15] Their average MPFB score was 22.6 ± 2.6 (mean ± s.d., population 18.9 ± 4.7) and their average MRT score was 15.0 ± 2.2

(population mean 9.1 ± 4.5). The five subjects tested therefore belonged to the top half of the population distribution for both tests. Each subject was free of neurological or psychiatric disorder, had a normal MRI brain scan and gave his written informed consent to take part in the project which had been approved by the Kremlin Bicêtre University Hospital Ethical Committee.

Task design: In the route learning session, each subject was driven to a suburban environment with which he was totally unfamiliar (see Fig. 1). This environment was selected because of its organization with both salient and different landmarks. The route was 800 m long: seven landmarks were selected, delimiting six segments along the route. The subject started to walk along the route and was asked to memorize both the visual aspects of the environment (including the seven landmarks that were pointed out and named by the experimenter) and the succession of locomotor action and orientation changes during the walk. The same itinerary was completed three times in a row, the walk duration between landmarks being recorded each time. During the first and third time, the subject was guided by the experimenter; the second time the subject walked the route under the experimenter's supervision.

The day after the learning session, and 4–6 h before PET data acquisition, the subjects were trained to execute the two mental tasks they were to perform during the PET session, namely mental simulation of routes (MSR) and visual imagery of landmarks (VIL). In the MSR task, the names of two landmarks were presented through earphones to indicate the route segment (departure first, arrival second) that the subject was required to mentally simulate. The subject was instructed to recall the visual and sensorimotor mental images of his walk along the segment. When the subject mentally reached the end of the segment, he had to press a button with his right index finger, this action releasing another pair of landmarks. This procedure was repeated until the subject had simulated the entire route three times. The duration of every mental simulation of route segment (mental route duration, MRD) was recorded.

In the VIL task, the subject was instructed to mentally visualize a landmark upon hearing its name through earphones and to maintain its mental image until he heard another landmark name 10 s later. This condition was intended to essentially involve static visual imagery.

PET session: Regional cerebral blood flow (rCBF) was measured six times for each subject, replicating a series of three conditions presented at random: MSR, VIL and Rest. The Rest condition, which was chosen as a second reference condition, consisted of resting silently. During the whole PET session the subject was lying in the camera with eyes closed, and a black opaque cloth covered the camera to turn it into a black chamber. Cognitive tasks started 30 s before the injection of labelled water and were sustained during scan acquisition. Following i.v. administration of 60 mCi ^{15}O-labelled water, a single emission scan of 80 s duration was acquired on an ECAT 953B/3116 with septa extended and reconstructed using the standard protocol of our laboratory.[13] Interscan interval was 15 min. During each condition, electro-oculogram (EOG) and heart rate (EKG) were recorded; MRD was measured during each MSR condition.

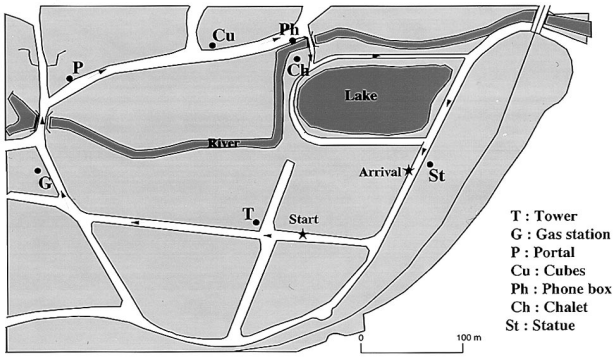

FIG. 1. Schematic map of the visited environment. Arrows indicate the route the subjects were to walk along. Landmarks to be memorized are indicated by their initials.

Data Analysis: Statistical parametric maps of the *t*-statistics corresponding to comparisons between MSR, VIL and Rest were generated with the 3D version of SPM[17] with global differences in CBF removed by scaling. Comparisons across conditions were made by way of *t*-statistics, three contrasts being analysed: MSR minus Rest, MSR minus VIL and VIL minus Rest. Corresponding Z volumes were projected in three orthogonal directions: sagittal, coronal and transverse, and thresholded at Z = 3.09 ($p < 0.001$, uncorrected for multiple comparisons). Due to the poor spatial resolution of SPM volumes, we could not resolve the different structures of the medial temporal lobe that belong or are close to the hippocampal formation. In the following, the hippocampal regions will thus designate the set of structures composed of the hippocampal formation, the entorhinal cortex and the parahippocampal gyrus.

Results

Chronometric results (Fig. 2): Strong correlations between average MRD and segment distances were observed both during the training session (r = 0.99,

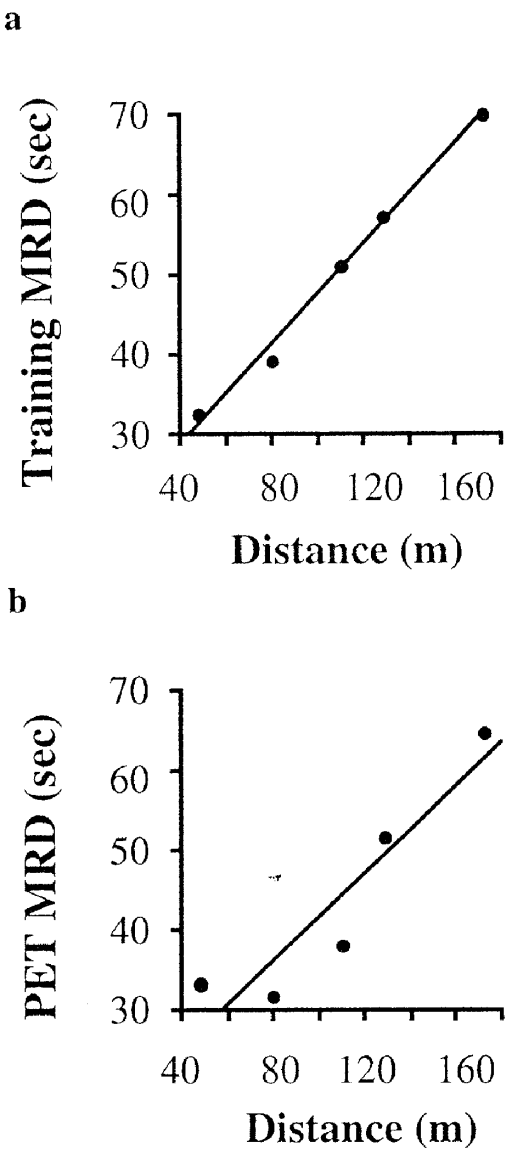

FIG. 2. Linear regression analysis between Mental Route Duration (MRD) and segments length during the training session (**a**) and during the PET session (**b**). MRD values were averaged across subjects for each segment.

$p = 0.0003$) and during the PET session ($r = 0.92$, $p = 0.024$). These results can be taken as indirect evidence that the subjects adequately executed the mental imagery task.[18]

EOG and EKG recordings: The amplitude of horizontal eye movements was significantly higher during MSR than during the other two tasks (ANOVA, $F = 12.31$; $df = 6,2$; $p = 0.007$), but their frequencies were not. Heart rate was significantly higher during VIL and MSR than during Rest (ANOVA, $F = 8.51$; $df = 6,2$; $p = 0.018$).

PET results: When compared with Rest, both MSR (Table 1, Fig. 3a) and VIL (Table 2, Fig. 3b) activated

Table 1. Foci of activation in the MSR condition minus Rest condition contrast ($n = 10$)

Anatomical location of maximal voxel	coordinates (mm)			Z-value	ΔrCBF (%)
	x	y	z		
L. dorsolateral prefrontal cortex	–22	50	4	4.36	3.34
R. dorsolateral prefrontal cortex	26	42	28	3.20	3.71
L. posterior hippocampal regions	–10	–44	4	4.21	7.1
R. posterior hippocampal regions	26	–32	–16	3.59	4.34
R. middle hippocampal regions	28	–18	–12	3.14	2.13
L. precuneus	–14	–70	36	4.14	6.13
L. precuneus	–4	–82	40	3.41	6.16
L. posterior cingulate gyrus	–14	–54	8	3.67	8.88
R. posterior cingulate gyrus	14	–56	8	3.19	6.23
Supplementary motor area	4	14	48	3.62	4.83
L. middle occipital gyrus	–30	–80	16	3.41	3.76
L. fusiform gyrus	–34	–40	–12	3.22	4.48
L. lateral premotor area	–34	–2	44	3.17	2.76
L. lateral Premotor Area	–26	0	52	3.10	2.51

Local maximal foci obtained at $p = 0.001$ confidence level uncorrected for multiple comparison. ΔrCBF (%) is the average percentage variation of the normalized rCBF at peak. L, left; R, right; n = number of scans for one condition.

Table 2. Foci of activation in the VIL condition minus Rest condition contrast ($n = 9$*)

Anatomical location of maximal voxel	coordinates (mm)			Z-value	ΔrCBF (%)
	x	y	z		
R. middle hippocampal regions	30	–18	–16	4.09	4.83
L. middle hippocampal regions	–32	–20	–12	3.16	4
L. posterior Hippocampal regions	–6	–42	4	3.14	4.11
R. posterior cingulate gyrus	18	–54	16	3.92	7.06
L. middle temporal gyrus	–50	–42	–12	3.53	4.02
L. middle temporal gyrus	–38	–4	–24	3.19	5.90
L. inferior temporal gyrus	–38	–14	–20	3.36	5.23
L. precentral gyrus	–48	2	8	3.17	2.6

Local maximal foci obtained at $p = 0.001$ confidence level uncorrected for multiple comparison. ΔrCBF (%) is the average percentage variation of the normalized rCBF at peak. L, left; R, right; n, number of scan for one condition. *Due to technical reasons only nine scans were recorded in VIL condition

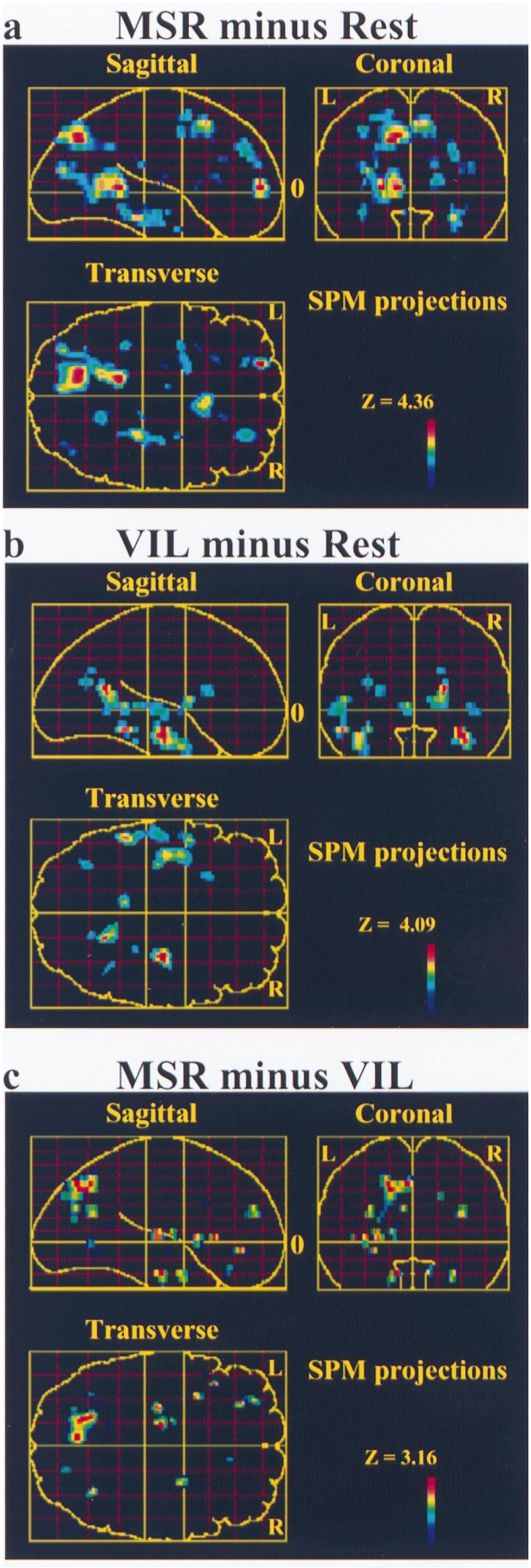

Table 3. Foci of activation in the MSR condition minus VIL condition contrast ($n = 9$*)

Anatomical location of maximal voxel	coordinates (mm)			Z-value	ΔrCBF (%)
	x	y	z		
L. medial hippocampal regions	−14	−18	−20	3.16	5.62
L. precuneus	−16	−70	36	3.14	6.33
L. insula	−40	18	4	3.13	2.55

Local maximal foci obtained at $p = 0.001$ confidence level uncorrected for multiple comparison. ΔrCBF (%) is the average percentage variation of the normalized rCBF at peak. L, left; R, right; *n*, number of scans for one condition. *Due to technical reasons only nine scans were recorded in VIL condition.

the middle part of the right hippocampal regions, the posterior part of the left hippocampal regions and the posterior cingulate gyrus, i.e. a region located at the inferior and posterior side of the splenium and corresponding to Brodmann's areas 23 and 30 according to the Talairach and Tournoux atlas.[19] Additional specific activations were found for each task: MSR activated the posterior part of the right hippocampal regions, the left middle occipital gyri, the left precuneus, the bilateral dorsolateral prefrontal areas and the supplementary motor area (SMA); VIL elicited additional activations in the middle part of the left hippocampal region and in the left middle and the left inferior temporal gyri. Finally, when compared with VIL, MSR elicited activations in the left hemisphere (Table 3, Fig. 3c), namely, the medial part of the left hippocampal regions, the left precuneus and the left insula.

Discussion

Task execution control: A major requirement in cognitive neuroimaging studies is to assess what the subjects really did during the task. In the present study, chronometric data were recorded in order to ensure that the subjects used mental imagery. Previous chronometric analyses have demonstrated positive correlations between distances and response times when subjects mentally simulated travel along routes using mental imagery, during both mental walking along routes[18] and mental scanning over

FIG. 3. Statistical parametric maps (SPM) of the comparison between the three tasks. (a) MSR *vs* Rest; (**b**) VIL *vs* Rest; (**c**) MSR *vs* VIL. SPMs are presented in three projections with the maximal pixel value showing the adjusted mean regional cerebral blood flow. The grid is the standard proportional stereotaxic grid into which all subject's brain scans were normalized. The antero-posterior commissural line is set at zero on the sagittal and coronal projections. Only pixels that were significantly different between task conditions are displayed with an arbitrary colour scale to indicate the maximal Z values. The minimal Z value was set at 2.58 (corresponding to $p = 0.005$) for display purposes.

geographical configurations.[20,21] We also found a strong correlation between MRD and actual distance, supporting the hypothesis that mental imagery was actually used by the subjects during MSR.

Functional anatomy: We propose that the cerebral structures found activated during the MSR task belong to two main networks, one involved in the memory component of the task and the other specific to mental navigation.

Activations of hippocampal regions, dorsolateral prefrontal cortex, posterior cingulate gyrus, and temporal regions reflect the participation of a memory network: In the MSR minus Rest contrast, the posterior part of the left and right hippocampal regions and the middle part of right hippocampal regions showed significant rCBF increases. The MSR task involves a complex set of spatial, multi-sensory, sequential, and contextual memory processes calling upon imagery that are usually considered as functions subserved by hippocampal regions. The medial temporal lobe is indeed well known to be involved in memory processes.[22] It is striking that, while the subjects of the present study had to simulate their routes without any perceptual stimuli, they activated hippocampal regions similar to those used for navigation encoding.[8,9] This can be explained by the analogy existing between the properties of mental images recalled during the MSR tasks and of the percepts involved during the encoding process. The VIL minus Rest contrast allowed us to specify which cerebral structures are involved in static visual imagery generated from memory, namely the middle part of hippocampal regions bilaterally and the posterior part of the left hippocampal regions. These activations overlap those belonging to the MSR minus Rest contrast. It is thus likely that the posterior-middle part of the hippocampal regions is tied to retention[23] and contextual memory,[7] two memory processes shared by both tasks.

We found bilateral prefrontal activations in the MSR minus Rest contrast, a result in agreement with a previous PET study that attributed to this region a role in the retrieval of complex pictorial information.[24] In the present study, this result indicates that this cortical region may subserve visual complex retrieval, and particularly its sequential structure.[25] Indeed, many PET studies have demonstrated the involvement of the prefrontal cortex in retrieval (see Ref. 26 for review). It is noteworthy that the dorsolateral prefrontal cortex was not significantly activated during VIL compared with Rest, which can be related to the lower memory load required by this task. This result fits well with another PET study showing that prefrontal activations are related to the effort of attempting to retrieve information from memory.[27]

The posterior cingulum was significantly activated during both MSR and VIL, consistent with the results of a recent fMRI study on navigation in a virtual environment[9] which reported activation of this region during both encoding and recognition. In addition, anatomical studies in monkeys have demonstrated the reciprocal connections between this region, the prefrontal areas and the hippocampus.[28] In the present study the posterior cingulum is likely to be recruited by reactivation from memory of one or several recollection components in a format similar to that used during encoding. More specifically, this region could be involved in the shared attentional effort over the different components required by the retrieval process common to both tasks, in agreement with a SPECT study postulating posterior cingulum recruitment by openness to external stimuli, as opposed to anterior cingulum activation by focused attention.[29]

Finally, the middle and inferior temporal regions were significanly activated in the VIL minus Rest contrast. Studies in both monkeys and humans (see Ref. 30 for review) have assigned different visual memory functions to the inferior temporal cortex, in particular the synthesis of object components into a unique configuration and the storage of object representation. As such, the inferior temporal cortex can be considered as a brain region where visual perception meets memory and imagery. Within this framework, it is likely that its activation during the VIL task reflects the recall of such 3D complex objects as landmarks.

Mental navigation is subserved by visual imagery and sensorimotor areas connected together by hippocampal regions: In the present study, the left middle occipital gyrus and precuneus were specifically activated during mental navigation. Activation of the middle occipital gyrus has already been described during mental visuo-spatial imagery[13] and visual long term memory[31] tasks.

The precuneus has also been reported to be activated during various visuo-spatial tasks[13,32,33] and has been hypothesized to subserve visual imagery during retrieval.[13,34] In agreement with these results, the visuo-spatial imagery and retrieval processes involved in the MSR task are likely to be at the origin of the left precuneus activation observed in the present study.

Additional specific activations during MSR were observed in SMA and the left insula. The SMA activation can be related, at least in part, to the mental imagery component of the task, a result in agreement with almost all neuroimaging studies dealing with mental imagery regardless of modality.[10,13,35]

Since the subjects had to press a button and moved horizontally their eyes with greater amplitude during the MSR task, it is difficult to attribute SMA activation to mental imagery only.[18] As regards activation of the insula, this region belongs to the paralimbic system which receives most of the inputs from monomodal and heteromodal sensory areas. In non-human primates the insula is a major relay of somatosensory information into the limbic system.[36] In addition, two recent PET studies have found the insula activated during vestibular stimulation[37] and body representation.[38] In our study, insula activation could be related to the mental evocation of the body position during the walk.

Finally, the medial part of the left hippocampal regions (part of Brodmann's area 28 or entorhinal cortex) was found activated in the MSR minus VIL contrast. Assuming that this contrast removes the static visual imagery and memory components from the MSR task, this result demonstrates that this region is specifically engaged in mental navigation, a result in agreement with numerous studies in rodents.[5] Neurophysiological studies, in particular, have emphasized the role of this structure and surrounding areas for navigation memory (see Ref. 7 for review). Navigation memory involves the internal simulation of acceleration, slowing down and turning, all actions generally associated with visual, vestibular and proprioceptive cues. It has been recently shown that hippocampal neurones in monkey and rat are influenced by whole body rotation and translation.[39] It has been also proposed that vestibular cues contribute to the role of hippocampus in navigation memory.[40,41] Therefore the medial part of hippocampal regions activation observed in our study may be related to the integration of multimodal dynamic spatial informations.

Conclusion

Mental 'replay' of navigation seems to be subserved by two distinct networks, one for long term memory reactivation that involves the posterior and middle hippocampal regions, the dorsolateral prefrontal cortex and the posterior cingulate gyrus, and the other for dynamic spatial mental imagery that involves the medial part of left hippocampal regions, visuospatial and sensorimotor areas. We postulate that the medial part of the left hippocampal regions connects visuospatial and body position informations to allow a coherent reconstitution of navigation.

References

1. Shemyakin FN. Psychological science in USSR. In: Ananyev BG ed. *Office of Technical Services, Report 62-11083*. Washington, DC, 1962: 86–255
2. Taylor HA and Tversky B. *Mem Cogn* **20**, 483–496 (1992).
3. Golledge RG. Environmental cognition. In: Stokols D and Atman I, eds. *Handbook of Environmental Psychology*. New York: John Wiley and Sons, 1987: 131–174.
4. Thorndyke PW and Hayes-Roth B. *Cogn Psychol* **14**, 560–581 (1982).
5. O'Keefe J and Nadel L. *The Hippocampus as a Cognitive Map*. London: Oxford University Press, 1978.
6. Eichenbaum H, Otto T and Cohen NJ. *Behav Brain Sci* **17**, 449–518 (1994).
7. Jarrard LE. *Behav Brain Res* **71**, 1–10 (1995).
8. Maguire EA, Frackowiak RSJ and Frith CD. *NeuroImage* **3**, S589 (1996). (Abstract)
9. Aguirre GK, Detre JA, Alsop DC *et al. Cerebr Cortex* 1047–3211 (1996).
10. Lang W, Petit L, Höllinger P *et al. NeuroReport* **5**, 921–924 (1994).
11. Decety J, Perany D, Jeannerod M *et al. Nature* **371**, 600–602 (1994).
12. Kosslyn SM, Alpert NM, Thompson WL *et al. J Cogn Neurosci* **5**, 263–287 (1993).
13. Mellet E, Tzourio N, Denis M *et al. J Cogn Neurosci* **7**, 433–445 (1995).
14. Likert A and Quasha WH. *Revised Minnesota Paper Form Board Test (Series AA)*. New York: The Psychological Corporation, 1941.
15. Vandenberg SG and Kuse AR. *Percept Motor Skills* **47**, 599–604 (1978).
16. Mazoyer B, Trebossen R, Deutch CM *et al. IEE Trans Med Imag* **10**, 499–504 (1991).
17. Friston KJ, Holmes AP, Worsley KJ *et al. Hum Brain Map* **2**, 189–210 (1995).
18. Decety J. *Cogn Brain Res* **3**, 87–93 (1996).
19. Talaraich J. and Tournoux P. *Co-planar stereotaxic atlas of the human brain*. Stuttgart: Thierme Verlag, 1988.
20. Kosslyn SM, Ball TM and Reiser BJ. *J Exp Psychol* **4**, 47–60 (1978).
21. Denis M, Gonçalves M-R and Memmi D. *Neuropsychologia* **33**, 1511–1530 (1995).
22. Squire LR and Zola-Morgan S. *Science* **253**, 1380–1386 (1991).
23. Mesulam MM. *Ann Neurol* **28**, 597–613 (1990).
24. Tulving E, Markowitsch HJ, Craik FIM *et al. Cerebr Cortex* **6**, 71–79 (1996).
25. Fuster JM. Memory and planning. Two temporal perspective of frontal lobe function. In: Jasper HH, Riggio S and Golgman-Rakic PS, eds. *Epilepsy and the Functional Anatomy of the Frontal Lobe*. New York: Raven Press, 1995: 9–20.
26. Buckner RL and Petersen S. *Semin Neurosci* **8**, 47–55 (1996).
27. Schacter DL, Alpert NM, Savage CR *et al. Proc Natl Acad Sci USA* **93**, 321–325 (1996).
28. Goldman-Rakic PS. *Annu Rev Neurosci* **11**, 137–157 (1988).
29. Ebmeier KP, Steele JD, MacKenzie DM *et al. Electroencephalogr Clin Neurophysiol* **95**, 434–443 (1995).
30. Miyashita Y. *Annu Rev Neurosci* **16**, 245–263 (1993).
31. Moscovitch M, Kapur S, Kohler S *et al. Proc Natl Acad Sci USA* **92**, 3721–3725 (1995).
32. Courteney SM, Ungerleider LG, Keil K *et al. Cerebr Cortex* **6**, 39–49 (1996).
33. Corbetta M, Miezin FM, Shulman GL *et al. J Neurosci* **13**, 1202–1226 (1993).
34. Fletcher PC, Dolan RJ and Frith CD. *Experientia* **51**, 1197–1207 (1995).
35. Jeannerod M. *Behav Brain Sci* **17**, 187–245 (1994).
36. Mesulam M-M and Mufson EJ. *J Comp Neurol* **212**, 38–52 (1982).
37. Bottini G, Sterzi R, Paulesu E *et al. Exp Brain Res* **99**, 164–169 (1994).
38. Bonda E, Petrides M, Frey S *et al. Proc Natl Acad Sci USA* **92**, 11180–11184 (1995).
39. O'Mara SM, Rolls ET, Berthoz A *et al. J Neurosci* **14**, 6511–6523 (1994).
40. Wiener S and Berthoz A. Forebrain structures mediating the vestibular contribution during navigation. In: Berthoz A, Gielen C, Henn V *et al*, eds. *Multisensory Control of Movement*. Vol. 1, New York: Oxford University Press, 1993: 427–456.
41. McNaughton BL, Chen LL and Markus EJ. *J Cogn Neurosci* **3**, 190–202 (1991).

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General Summary
Modern neuroimaging was used to study in humans the neurobiological substrate of a basic animal behaviour, namely navigation. Normal volunteers walked in a natural environment and were requested to memorize all aspects of the itinerary. One day later, images of their brain were obtained with a positron camera while they mentally reproduced this itinerary. Two distinct systems appear to subserve this mental activity, one for long term memory, the other responsible for the generation of the complex sequences of mental images required for mental navigation.