Human spatial navigation: cognitive maps, sexual dimorphism, and neural substrates

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Recent research on navigation has been particularly notable for the increased understanding of the factors affecting human navigation and the neural networks supporting it. The use of virtual reality environments has made it possible to explore the effect of environment layout and content on way-finding performance, and it has shown that these effects may interact with the sex and age of subjects. Functional brain imaging, combined with the use of virtual environments, has revealed strong parallels between humans and other animals in the neural basis of navigation.

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Abbreviations
fMRI   functional magnetic resonance imaging
PET   positron emission tomography

Introduction

The study of navigation has a long history in neuroscience. The course of its investigation is marked by a number of key events, not least of which took place over fifty years ago with Tolman's assertion [1] that rats have cognitive maps of the spatial layout of their environments. Several decades later, the discovery of place cells — pyramidal cells in the rat hippocampus with location-specific activity [2] — provided physiological grounding for the study of navigation. Since then, much has been learned about navigation in rodents [3,4,5•,6,7] and birds [8••,9]. Recent studies have also begun to elucidate the neural representation of allocentric (world-centred) spatial locations in the hippocampus [10•,11•] and posterior parietal cortex [12•] of monkeys.

In this review, we address the issue of how much of this applies to human navigation. The past year or so is notable in witnessing a convergence of findings across species and methodologies, with increased understanding of human navigation particularly evident. Recent investigations have examined the roles of three important variables involved in human navigation research: the stimuli employed to examine navigation and their manipulation; the sex and age of the human subjects; and the neural network supporting navigation and possible functions of its key elements.

Embracing the real world, virtually

One of the major steps forward in the past year in the neuroscience of human navigation is the widespread acknowledgement that navigation is not the same as table-top tests of spatial memory (but see [13•]) and that direct inferences cannot be made about one from the other. Not only do they differ in terms of the perspective from which the observer is required to operate (i.e. viewer-centred during navigation compared to an aerial perspective in table-top/geographical knowledge tasks), but, arguably, also in their frames of reference (i.e. allocentric in navigation and egocentric in table-top tasks). On the table-top, all information is within one field of view; this is not the case in a complex environment through which one has to navigate where much of the relevant information is unseen. Patients with topographical memory deficits, who are unimpaired on table-top spatial/geographical knowledge tests, have been described in the literature [14,15]. The opposite type of impairment has also been observed recently. Maguire and Cipolotti [16•] reported the case of a patient with selective preservation of navigation ability in the context of profound verbal and visual memory deficits and poor geographical knowledge, confirming the double dissociation between navigation and table-top spatial tasks.

In order to capture the true dynamism of real navigation while maintaining some degree of stimulus control, computer-simulated or virtual reality environments have been widely used in the past year to study navigation. Primarily, this has involved the use of non-immersive (monitor-displayed) virtual environments. There are issues surrounding the representation of virtual compared to physically real space: the field of view is typically narrower than that available in the real world and detail resolution may be reduced; navigation is performed on the basis of visual information with an absence of vestibular or proprioceptive information; and subjects must become familiar with the use of a mouse/keypad to direct movement. Despite current limitations [17], it has been shown that cognitive maps built up in virtual environments are comparable to those acquired in the real environment [18•]. Recent studies have also confirmed that representations of large-scale space learned in virtual environments are transferred when subjects subsequently navigate in the real place [19–22]. Held and Durlach [23] suggest that an important advantage of virtual reality is that it elicits a strong sense of 'presence' compared to table-top tests. Defining 'presence' as the subjective experience of being in one place when one is physically in another, Witmer and Singer [24] found significant correlations between 'presence' and performance in virtual environments.

Figure 1
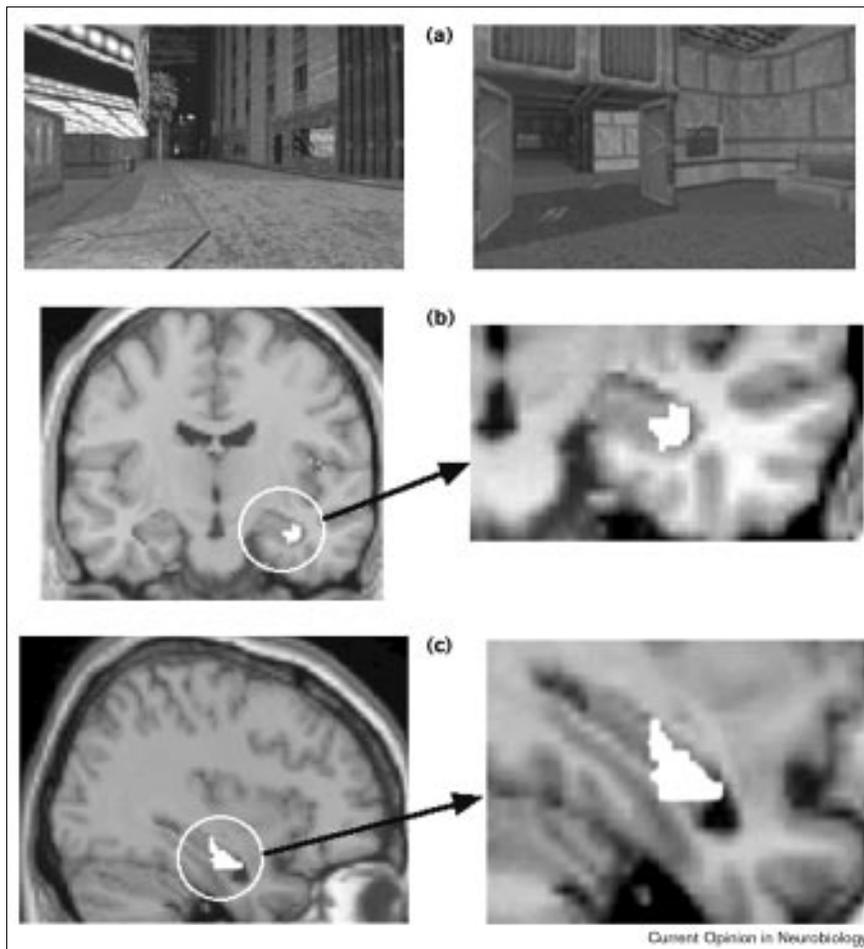
Activation of the right hippocampus during navigation. **(a)** Scenes from the virtual town used by Maguire *et al.* [63••]. Subjects navigated through the town, which they viewed in colour. **(b)** PET scans showing the location of the increased activity in the right hippocampal formation associated with increased accuracy of navigation in the virtual town. The full coronal section is shown on the left, with a magnified view of the right medial temporal region on the right-hand side. **(c)** The same activation is shown in a sagittal section, again with the medial temporal region magnified on the right-hand side.

In one line of research, there have been attempts to examine human place learning in virtual environments by mirroring previous rodent work. Jacobs *et al.* [25•] replicated the Morris water maze test [26] by using a hidden platform in a virtual circular arena within a square room. They found that subjects learned the position of the hidden platform on the basis of distal cues alone, and that the use of distal cues was not disengaged by the presence of proximal cues. Subjects were also able to generalise place learning from familiar to novel start locations. A related finding in rats shows that while the orientation of the place cell representation of space depends on distal visual cues, it does not depend on intramaze cues [27]. Interestingly, while hippocampal lesions impair rats' ability to return to a hidden platform located relative to the constellation of distal cues [28], they do not impair their ability to return to a hidden platform located at a fixed bearing from a single intramaze cue [29•].

In a further set of experiments, Jacobs *et al.* [30•] removed sets of distal cues (which covered whole walls) and observed the effect on place learning. They found that removing cues from one, two or three out of four distal walls

did not significantly disrupt the ability of human subjects to relocate a place. These findings are concordant with findings reported for place learning by rats in a Morris water maze [31]. Cognitive mapping theory predicts that changes in the topological relations among distal cues rather than a decrease in their number will disrupt place learning [3]. This was found to be the case in rats [32–34], and now Jacobs *et al.* [30•] report it in humans where place learning in the virtual environment was disrupted by changes to the relations among distal landmarks, confirming that cognitive mapping operates in humans as well as rats.

The effect on navigational performance of manipulating the objects, textures and landmarks in an environment has been a strong feature of much research into navigation in virtual environments. As well as place learning in a convex arena, other studies have used more complex virtual environments to study navigation between different places on a larger scale (see e.g. [18•,20,35•,36]). Ruddle *et al.* [18•] found that route-finding accuracy was not improved by the use of abstract coloured patterns as landmarks; however, when familiar objects were used as landmarks instead, route-finding accuracy improved compared to a no-landmark condition.

Previously, it has been shown that the route through a series of linked identical rooms with two possible exits in each room could be learned better if landmarks were associated with the correct door compared to when they were not [37]. Interestingly, however, this effect was only apparent if subjects in the no-landmark condition were required to engage in a verbal interference task, which prevented them from employing a left/right list-learning strategy.

These studies reveal several important points about navigation. Firstly, they confirm the importance of landmarks as major constituents of spatial representations (see [38]). Secondly, they demonstrate the importance of 'presence' in stimulus environment — landmarks need to be realistic if they are to be used by the navigator in more complex environments. Thirdly, it is clear that the design of simulated environments, the level of differentiation, the number of choice points [36], the placement of landmarks and their orientation [18•] require careful consideration so as to engage as much as possible the cognitive processes that are used in navigation in real, complex large-scale spaces.

Navigation: a sexually dimorphic skill?
The points discussed above are relevant to another strand of navigation research assessing whether navigation performance is sensitive to gender. Several studies using computer-simulated environments have found male advantages in navigation performance using either landmark-free or landmark-limited environments [13•,39]. A study by Sandstrom *et al.* [40••] probes the navigation strategies of both sexes. By manipulating the availability of geometric cues and landmarks as distal cues in a virtual water maze environment, they found that female subjects rely predominantly on landmark cues whereas males use both geometric and landmark cues. Male advantages on virtual maze tasks must be interpreted in the light of these findings, and underlines the need to prevent biasing of environmental construction towards one strategy/cue type over another, or at least balancing the representation of the sexes in subject samples during navigation experiments. This work in virtual environments echoes findings in the real world, where similar differences between the sexes have been found [41,42]. In rats, there are also reports of males attending primarily to the global shape of the environment, whereas females consider this and landmark cues in addition [43].

The possible bases of sex differences in navigation have been interpreted in evolutionary terms (see [13•,44]). However, in a recent study by Schmitz [45•] of way-finding by boys and girls aged 10–17 years in a real environment, girls scored higher on fear and anxiety scales than boys and moved more slowly through the environment than boys, but showed no overall difference in the total number of elements recalled. Such data, coupled with the acknowledged greater experience of males on video games reported in several studies [13•,39,40••], must also be factored into the complex interaction between the characteristics of the environment and those doing the navigating.

As well as possible sex differences, studies have revealed how the ability to navigate changes throughout development. Hermer and Spelke [46], and more recently Hermer [47••], have shown that children below 5.5 years of age have internally consistent representations of object locations, but rely on the geometrical properties of an environment (in this case a room) for reorientation, even in the presence of a distinctive physical cue. This finding may have parallels with reports of the preferential responsiveness of rats' place cells to geometric properties of environments [48]. In contrast to young children, adult humans were found to take account of nongeometric as well as geometric information to aid orientation [47••].

Neural substrates of navigation
Much work in the past year has gone into exploring further the neural basis of navigation in humans. Just as the layout, complexity and content of environments affect navigation performance and interact with the sex and age of subjects, so might environmental and subject factors interact with the neural mechanisms supporting navigation. Very little is yet known about the neuroanatomical differences, if any, that are associated with sex or age differences and human navigation. In contrast, the effects of environmental manipulations have been examined by functional imaging studies in which subjects navigate in virtual environments during PET or fMRI scanning. Neuroimaging provides unique insights into the networks of brain regions supporting navigation in the normal human brain *in vivo*. A consistent pattern of brain activity associated with navigation has emerged from imaging work in the past year or so, but there are still some disagreements about the exact functions of particular elements of the navigation system. From recent imaging work it seems clear that key regions for navigation in humans include the medial and right inferior parietal cortex, the posterior cingulate cortex, parts of the basal ganglia, the left prefrontal cortex, the bilateral medial temporal region (including the parahippocampal gyrus) and the hippocampus proper. Disagreement surrounds the role of the medial temporal region in particular.

Using fMRI scanning, Aguirre *et al.* [49] have reported that navigation in a virtual maze is associated with increased activity in the parahippocampal gyrus but not in the hippocampus, giving rise to the suggestion that, unlike rats, the parahippocampal gyrus but not the hippocampus is the crucial neural structure supporting spatial mapping in humans [50]. Other imaging studies, however, suggest a different role for the parahippocampal gyrus. This area is active when recalling landmarks, but not when recalling complex routes where the use of a cognitive map would be required [51•]. A PET study found that the parahippocampal gyrus is activated when the recall of object location in a spatial array is required, akin to traditional table-top tasks [52]. Passive processing of scenes [53•,54•] also activate this area.

This evidence points to a role for the parahippocampal gyrus and posterior occipito-temporal cortex [55•] in

object–location associations (as in the monkey, see [56]), but not more complex cognitive mapping. Further evidence of this comes from a PET study in which navigation in a stark featureless virtual maze-like environment was compared to navigation in a maze-like environment that included several everyday objects as landmarks. The parahippocampal gyrus was activated only when navigation occurred in the maze with landmarks ([57•]; but see [53•]). Thus, just as landmarks were found to have an impact on way-finding in the behavioural studies described above, their presence is also an influential factor on the neural mechanisms supporting navigation. A recent report of patients with selective bilateral damage restricted to the hippocampus (and where the surrounding cortex was intact) found that, as well as having impaired episodic memory, these patients are also unable to find their way around, despite having an intact parahippocampal cortex [58••]. This suggests that representing large-scale space depends on the human hippocampus proper, either directly, or at least via its role in episodic memory [59,60].

The imaging work just described also highlights a further effect of environmental manipulation, with implications for the brain regions activated. In scanning studies using simple maze-like environments [49,57•], there was no increased activation of the hippocampus proper. We believe that these environments, limited in their range of texture, number of choice points and arrangements of landmarks, may have two drawbacks in relation to study of the hippocampus. They do not feel realistic (i.e. they have poor 'presence'), and they can be amenable to solution without recourse to a cognitive map (e.g. by using a linear or verbal representation). This stands in contrast to the increases in hippocampal activity observed when subjects learned how to navigate through a town by watching film footage of travel through a real town [61], by recalling routes through a real city [51•], or by recalling a route learned in the real world before scanning took place [62•]. Taking these findings into consideration, scanning experiments are now using more realistic town-like environments to simulate real navigation with increased 'presence'. The opportunity afforded by being able to combine monitoring changes in blood flow with recording and measuring online navigation performance has given further insights into the precise activity of elements of the navigation network.

Recently, we used PET to scan subjects while they performed retrieval tasks in a complex computer-simulated town they had spent time learning prior to scanning [63••] (see Figure 1). Subjects either found their way to specified destinations in the town using the internal representation they built up during learning or followed a trial of arrows through the town that did not require the use of topographical memory but controlled for movement and optical flow. Subjects' behavioural performances as well as changes in cerebral perfusion during scanning were recorded and analysed. The right hippocampus was more activated when reaching a destination successfully than when following the

trail of arrows, and during successful trials than during unsuccessful trials. This latter finding was also true for the left hippocampus. In addition, there was a significant correlation between blood flow changes in the right hippocampus and right inferior parietal cortex with the accuracy of navigation — the more accurate the path taken to the goal place, the more active these regions. The highest correlation was found in the right hippocampus and the second highest in the right inferior parietal cortex.

We interpret these findings to mean that the output of the hippocampus on the right side is a vector that continuously points to the goal location, a finding consistent with a model of the rat hippocampus (see [64]). The lower correlation in the parietal cortex may reflect its response to other variables, such as egocentric trunk/head position information. Activity in the left hippocampus, although associated with successful navigation, did not covary significantly with the measure of navigation accuracy. This means that it is involved in navigation but in a way different from the right hippocampus. Lesions to either the left or the right medial temporal regions in humans are known to affect navigation ([65]; see also [66]), although lesions on the right are more generally associated with impairments to spatial memory [67,68••]. Perhaps the left hippocampus has a less specifically spatial role (e.g. verbal) in memory that is useful in navigation nonetheless.

Which part of the hippocampus is associated with navigation?

From a recent meta-analysis of PET studies that have activated the hippocampal region, Lepage *et al.* [69•] suggest that activations associated with memory encoding are located primarily in the anterior portion of the hippocampus, whereas retrieval activations are located more posteriorly. They have called this the HIPER (hippocampal encoding/retrieval) model. Imaging of navigation does not fit with this model, with both encoding and retrieval typically associated with activation of more posterior portions of the hippocampal region. The inclusion criteria for the meta-analysis were somewhat arbitrary and another meta-analysis study found a less clear-cut distinction [70•]. Nevertheless, the navigation imaging findings do fit with rat studies where it has been shown that damage to the dorsal third of the rat hippocampus, but not lesions to the ventral two thirds, is sufficient to cause severe impairments on the Morris water maze task [71]. Recent rodent studies continue to explore the dorsal/ventral distinction [72,73], which is perhaps equivalent to the posterior/anterior distinction in humans. Bohbot *et al.* [68••] examined epilepsy surgery patients and found that four out of six patients with right hippocampal lesions, who were unimpaired on a spatial task modelled on the Morris water maze, had intact posterior portions of the right hippocampus. More work is needed to examine this more closely in humans, paying particular attention to the remnant of hippocampal tissue and its fate in the months following epilepsy surgery [74].

Conclusions

Recent work examining human navigation has employed more realistic stimuli, often in the form of virtual reality environments, to characterise the cognitive processes engaged during dynamic way-finding in large-scale space. The complexity and content of the environment affects navigation success and may also interact with the sex and age of the subjects being tested. The nature of the environment also impacts upon the neural mechanisms required to support navigation. It is not possible on the basis of the data gathered so far to determine how the hippocampal formation and the parietal cortex interact during human navigation (see [75••]) nor the precise inputs and outputs of the human navigation system in general. Currently, there are limitations to virtual environments; as mentioned previously, they lack the requirement for vestibular inputs that take place during real navigation [6,76]. Future technologies will need to address this. Nevertheless, the past year has demonstrated that humans can navigate in complex virtual environments with solely visual stimulation and that the function of the right human hippocampus has strong parallels with hippocampal function in navigating rats and other animals. Precisely how the role of the hippocampus in navigation dovetails with its acknowledged importance in the wider context of episodic memory [59,60] has been the subject of speculation (e.g. [3,75••]), but remains a critical issue for future research.

Acknowledgements

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest
•• of outstanding interest

1. Tolman EC: **Cognitive maps in rats and man.** *Psychol Rev* 1948, **55**:189-208.

2. O'Keefe J, Dostrovsky J: **The hippocampus as a spatial map: preliminary evidence from unit activity in the freely-moving rat.** *Brain Res* 1971, **34**:171-175.

3. O'Keefe, Nadel L: *The Hippocampus as a Cognitive Map.* Oxford: Clarendon Press; 1978.

4. Muller RU: **A quarter of a century of place cells.** *Neuron* 1996, **17**:813-822.

5. Taube JS: **Head direction cells and the neuropsychological basis**
•   **for a sense of direction.** *Prog Neurobiol* 1998, **55**:225-256.
A thorough review of *in vivo* electrophysiological studies in rats showing cells coding explicitly for the animal's head direction. The relationship of these findings to human's sense of direction is explored briefly.

6. McNaughton BL, Barnes CA, Gerrard JL, Gothard K, Jung MW, Knierim JJ, Kudrimoti H, Qin Y, Skaggs WE, Suster M, Weaver KL: **Deciphering the hippocampal polyglot: the hippocampus as a path integration system.** *J Exp Biol* 1996, **199**:173-185.

7. Lipp HP, Wolfer DP: **Genetically modified mice and cognition.** *Curr Opin Neurobiol* 1998, **8**:272-280.

8. Claydon NS, Dickinson A: **Episodic-like memory during cache**
•• **recovery by scrub jays.** *Nature* 1998, **395**:272-274.
A demonstration of all the elements of episodic memory in food-storing birds. The existence of something analogous to episodic memory in nonhumans has been notoriously hard to prove. In this study, recall of the time, place and content of an event (e.g. caching of the food) could be inferred from the behaviour of the birds in retrieving two types of stored food, one of which decays faster than the other.

9. Sherry DF, Duff SJ: **Behavioural and neural basis of orientation in food-storing birds.** *J Exp Biol* 1996, **199**:165-172.

10. Robertson RG, Rolls ET, Georges-Francois P: **Spatial view cells in**
•   **the primate hippocampus: effects of removal of view details.** *J Neurophysiol* 1998, **79**:1145-1156.
This study describes cells in region CA1 of primate hippocampus that respond whenever the monkey looks at a particular location in the testing room, independent of its visual characteristics (e.g. tested by drawing a curtain across it or switching off the lights).

11. Nishijo H, Ono T, Eifuku S, Tamura R: **The relationship between**
•   **monkey hippocampus place-related neural activity and action in space.** *Neurosci Lett* 1997, **226**:57-60.
Reports place-related neural activity in the primate hippocampal formation when the monkey controls its own movements around the testing room (on a robot), but not when the experimenter controls the movements.

12. Snyder LH, Grieve KL, Brotchie P, Andersen RA: **Separate body- and**
•   **world-referenced representations of visual space in parietal cortex.** *Nature* 1998, **394**:887-891.
Recording from neurons in area 7a of monkey posterior parietal cortex, the authors observed 'gain-field' modulation of the animal's response to a visual stimulus encoding the stimulus location in the testing room. This contrasts with gain-field encoding of the location of the stimulus relative to parts of the body (e.g. trunk, head, etc.) in other parietal areas. Interestingly, area 7a is the part of parietal cortex with strong projections to the parahippocampal and presubicular cortices.

13. Moffat SD, Hampson E, Hatzipanteli: **Navigation in a 'virtual' maze:**
•   **sex differences and correlation with psychometric measures of spatial ability in humans.** *Evol Hum Behav* 1998, **9**:73-87.
Male and female human subjects learned to take a route through a corridor-based, landmark-free virtual reality maze over five trials. A significant advantage was found for male performance in terms of the number of errors committed and time taken, despite correction for the males' extra experience of similar computer games.

14. McCarthy RA, Evans JJ, Hodges JR: **Topographic amnesia: spatial memory disorder, perceptual dysfunction, or category specific semantic memory impairment?** *J Neurol Neurosurg Psychiatry* 1996, **60**:318-325.

15. Habib M, Sirigu A: **Pure topographical disorientation: a definition and anatomical basis.** *Cortex* 1987, **23**:73-85.

16. Maguire EA, Cipolotti L: **The selective sparing of topographical**
•   **memory.** *J Neurol Neurosurg Psychiatry* 1998, **65**:903-909.
The authors report a patient in the advanced stages of Pick's disease who showed severely impaired recall and recognition of verbal and visual material on standard tests including geographical knowledge, but spared landmark and scene recognition and preserved ability to navigate through large-scale spaces. This demonstrates the double dissociation between navigation and table-top spatial tasks.

17. Peruch P, Gaunet F: **Virtual environments as a promising tool for investigating human spatial cognition.** *Curr Psychol Cogn* 1998, **17**:881-899.

18. Ruddle RA, Payne SJ, Jones DM: **Navigating buildings in 'desk-top'**
•   **virtual environments: experimental investigations using extended navigational experience.** *J Exp Psychol* 1997, **3**:143-159.
Shows that, with practice, people can learn to navigate inside a simulated building as accurately as in the real building. The addition of everyday objects as landmarks improved performance, whereas cubes with abstract coloured patterns on them did not (an interesting parallel to findings reported in [57•]).

19. Regian JW, Yadrick RM: **Assessment of configurational knowledge of naturally- and artificially-acquired large-scale space.** *J Environ Psychol* 1994, **14**:211-223.

20. Witmer BG, Bailey JH, Knerr BW: **Virtual spaces and real world places: transfer of route knowledge.** *Int J Human-Computer Studies* 1996, **45**:413-428.

21. Arthur EJ, Hancock PA, Chrysler ST: **The perception of spatial layout in real and virtual worlds.** *Ergonomics* 1997, **40**:69-77.

22. Waller D, Hunt E, Knapp D: **The transfer of spatial knowledge in virtual environment training.** *Presence* 1998, **7**:129-143.

23. Held R, Durlach N: **Telepresence.** *Presence* 1992, **1**:109-112.

24. Witmer BG, Singer MJ: *Measuring Presence in Virtual Environments. ARI Technical Report 1014.* Alexandria, Virginia: US Army Research Institute for the Behavioral and Social Sciences; 1994.

25. Jacobs WJ, Laurance HE, Thomas KGF: **Place learning in virtual**
• **space. I. Acquisition, overshadowing, and transfer.** *Learn Motiv* 1998, **28**:521-541.
This study, and a follow-up study [30•], shows that human subjects can learn a virtual reality version of the Morris water-maze using only distal visual cues. Consistent with the idea that subjects form a cognitive map of the maze, the authors found that the subjects took short cuts from novel start locations and that their performance was unimpaired by removal of subsets of the distal visual cues but was impaired by rearrangement of the cues or removal of all of them.

26. Morris RGM: **Spatial localization does not require the presence of local cues.** *Learn Motiv* 1981, **12**:239-260.

27. Cressant A, Muller RU, Poucet B: **Failure of centrally-placed objects to control the firing fields of hippocampal place cells.** *J Neurosci* 1997, **17**:2531-2542.

28. Morris RGM, Garrard P, Rawlins JNP, O'Keefe J: **Place navigation impaired in rats with hippocampal lesions.** *Nature* 1982, **297**:681-683.

29. Pearce JM, Roberts ADL, Good M: **Hippocampal lesions disrupt**
• **navigation based on cognitive maps but not heading vectors.** *Nature* 1998, **396**:75-77.
Reports that hippocampal lesions do not impair a rat's performance in returning to the hidden platform in the Morris water maze when its location is defined by a directional bearing from a single intramaze cue, but they do impair performance in the standard set-up in which the location is defined relative to the constellation of distal cues.

30. Jacobs WJ, Thomas KGF, Laurance HE, Nadel L: **Place learning in**
• **virtual space. II. Topographical relations as one dimension of stimulus control.** *Learn Motiv* 1998, **29**:288-308.
See annotation [25•].

31. Fenton AA, Arolfo MP, Nerad L, Bures J: **Place navigation in the Morris water maze under minimum and redundant extra-maze cue conditions.** *Behav Neural Biol* 1994, **62**:178-189.

32. O'Keefe J, Conway DH: **Hippocampal place units in the freely moving rat: why they fire where they fire.** *Exp Brain Res* 1978, **31**:573-590.

33. Suzuki S, Augerinos G, Black AH: **Stimulus control of spatial behavior on the eight-arm radial maze.** *Learn Motiv* 1980, **11**:1-8.

34. Pico RM, Gerbrandt LK, Pondel M, Ivy G: **During stepwise cue deletion, rat place behaviors correlate with place unit responses.** *Brain Res* 1985, **330**:369-372.

35. Gillner S, Mallot HA: **Navigation and acquisition of spatial**
• **knowledge in a virtual maze.** *J Cogn Neurosci* 1998, **10**:445-463.
Shows that humans can form a cognitive-map-like representation of space from the local visual information available during exploration of a virtual reality town. The subjects demonstrated an ability to generate novel routes and short-cuts, estimate the distances between places, and draw a bird's-eye plan of the town.

36. Ruddle RA, Payne SJ, Jones DM: **Navigating large-scale 'desk-top' virtual buildings: effects of orientation aids and familiarity.** *Presence* 1998, **7**:179-192.

37. Tlauka M, Wilson PN: **The effect of landmarks on route-learning in a computer-simulated environment.** *J Environ Psychol* 1994, **14**:305-313.

38. Siegal AW, White SH: **The development of spatial representations of large-scale environments.** In *Advances in Child Development and Behavior*, vol 10. Edited by Reese H. New York: Academic Press; 1975:10-55.

39. Astur RS, Ortiz ML, Sutherland RJ: **A characterization of performance by men and women in a virtual Morris water task: a large and reliable sex difference.** *Behav Brain Res* 1998, **93**:185-190.

40. Sandstrom NJ, Kaufman J, Huettel SA: **Males and females use**
•• **different distal cues in a virtual environment navigation task.** *Cogn Brain Res* 1998, **6**:351-360.
Male and female subjects learned a virtual reality version of a Morris water maze that contained distal visual cues within a trapezoidal room. When tested with the same cues within an octagonal room, male and female subjects did not show a significant difference in performance. However, removing the distal cues, or varying their locations randomly, impaired the performance of females significantly more than the males, who were better able to make use of the trapezoidal shape of the room.

41. Galea LAM, Kimura D: **Sex differences in route-learning.** *Pers Individ Differ* 1992, **14**:53-65.

42. Lawton CA: **Gender differences in way-finding strategies: relationship to spatial ability and spatial anxiety.** *Sex Roles* 1994, **30**:765-779.

43. Williams CL, Meck WH: **The organizational effects of gonadal steroids on sexually dimorphic spatial ability.** *Psychoneuroendocrinology* 1991, **16**:155-176.

44. Dabbs JM Jr, Chang E-L, Strong RA, Milun R: **Spatial ability, navigation strategy, and geographic knowledge among men and women.** *Evol Human Behav* 1998, **19**:89-98.

45. Schmitz S: **Gender-related strategies in environmental**
• **development: effects of anxiety on wayfinding in and representation of a three-dimensional maze.** *J Environ Psychol* 1997, **17**:215-228.
Girls and boys aged 10–17 years old explored a maze-like environment arranged in a large building over two floors. Anxiety was assessed prior to the task, and task-specific fear was assessed during the task. Subjects explored the maze five times. Following run four, they had to draw or write representations of the maze. Overall, girls were more anxious and fearful than boys and were slower to move through the maze. Interestingly, no sex differences emerged in the number of maze elements recalled. In general, subjects who were more anxious and fearful traversed the maze more slowly and remembered more landmarks but fewer directions than less anxious subjects.

46. Hermer L, Spelke ES: **A geometric process for spatial reorientation in young children.** *Nature* 1994, **370**:57-59.

47. Hermer L: **Internally coherent spatial memories in a mammal.**
•• *Neuroreport* 1997, **8**:1743-1747.
When searching for an object hidden in the corner of a rectangular room, young children will search in both geometrically correct corners despite a disambiguating wall [46]. This paper examined the errors in recalling the location of two hidden objects and the door. These errors tended to be self-consistent, indicating that the spatial representation used relies upon a unitary sense of direction determined by the geometry of the room (see [5•] for a possible neural basis for this).

48. O'Keefe J, Burgess N: **Geometric determinants of the place fields of hippocampal neurons.** *Nature* 1996, **381**:425-428.

49. Aguirre GK, Detre JA, Alsop DC, D'Esposito M: **The parahippocampus subserves topographical learning in man.** *Cereb Cortex* 1996, **6**:823-829.

50. Aguirre GK, Zaharn E, D'Esposito M: **Neural components of topographical representation.** *Proc Natl Acad Sci USA* 1998, **95**:839-846.

51. Maguire EA, Frackowiak RSJ, Frith CD: **Recalling routes around**
• **London: activation of the right hippocampus in taxi drivers.** *J Neurosci* 1997, **17**:7103-7110.
A PET study in which taxi drivers described either routes between locations in London, famous landmarks, film plots or individual frames from films. The route and landmark conditions were associated with bilateral parahippocampal activation compared to a control condition, with the route condition also showing activation of the right hippocampus compared to control condition (or any other condition).

52. Owen AM, Milner B, Petrides M, Evans AC: **A specific role for the right parahippocampal gyrus in the retrieval of object-location: a positron emission tomography study.** *J Cogn Neurosci* 1996, **8**:588-602.

53. Epstein R, Kanwisher N: **A cortical representation of the local**
• **visual environment.** *Nature* 1998, **392**:598-601.
A fMRI study showing greater bilateral activation of a parahippocampal/fusiform region when subjects viewed scenes than when they viewed objects or jumbled up scenes (see [55•] for a description of similar results). Subjects were not required to learn or remember any of the stimuli. The response to indoor scenes depended on the presence of the walls of the room being in the correct configuration (consistent with place-cell recordings in rat hippocampus that indicate the external walls of the environment as the most significant input; see [48]).

54. Aguirre GK, D'Esposito M: **Environmental knowledge is subserved**
• **by separable dorsal/ventral neural areas.** *J Neurosci* 1997, **17**:2512-2518.
A fMRI study in which, having explored a virtual reality town, subjects had to recognise the location of a particular view or indicate the egocentric direction of a target location from the current view. Bilateral parahippocampal activity was observed in both tasks relative to a control condition. The direction task was associated with greater parietal activation, and the recognition task with greater lingual, fusiform and parahippocampal activation.

55. Aguirre GK, Zaharn E, D'Esposito M: **An area within human ventral**
• **cortex sensitive to 'building' stimuli: evidence and implications.** *Neuron* 1998, **21**:373-383.
A fMRI study showing greater activation of a region straddling the lingual sulcus bilaterally when subjects viewed buildings than when they viewed faces,

everyday objects or scrambled buildings (see [53•] for a description of similar results).

56. Suzuki WA, Miller E, Desimone R: **Object and place memory in the macaque entorhinal cortex.** *J Neurophysiol* 1997, **78**:1062-1081.

57. Maguire EA, Frith CD, Burgess N, Donnett JG, O'Keefe J: **Knowing**
•   **where things are: parahippocampal involvement in encoding object locations in virtual large-scale space.** *J Cogn Neurosci* 1998, **10**:61-76.
A PET study of the exploration of virtual environments. Right parahippocampal activation was observed during exploration of a richly textured environment containing everyday objects, but not during exploration of a plain maze of empty rooms and corridors.

58. Vargha-Khadem F, Gadian DG, Watkins KE, Connolly A, Van
••   Paesschen W, Mishkin M: **Differential effects of early hippocampal pathology on episodic and semantic memory.** *Science* 1997, **277**:376-380.
A study of three patients with bilateral hippocampal pathology (but apparent sparing of the surrounding cortical tissue) caused by anoxic events early in life. These patients showed remarkably spared factual knowledge and recognition memory, but strongly impaired episodic memory in everyday life. While not conclusive, this study indicates that the hippocampus is required for episodic memory, but not necessarily required for semantic or recognition memory.

59. Milner B: **Disorders of learning and memory after temporal lobe lesions in man.** *Clin Neurosurg* 1972, **19**:421-446.

60. Tulving E: *Elements of Episodic Memory*. Oxford: Clarendon Press; 1983.

61. Maguire EA, Frackowiak RSJ, Frith CD: **Learning to find your way — a role for the human hippocampal region.** *Proc R Soc Lond [Biol]* 1996, **263**:1745-1750.

62. Ghaem O, Mellet E, Crivello F, Tzourio N, Mazoyer B, Berthoz A, Denis
•   M: **Mental navigation along memorized routes activates the hippocampus, precuneus, and insula.** *Neuroreport* 1997, **8**:739-744.
A PET study in which subjects either imagined walking along a segment of a path they had walked the day before, or imagined the appearance of a landmark seen from the route. Both tasks activated a network of brain regions compared to rest, including right and left hippocampal areas. The mentally simulated walking activated left medial hippocampal regions compared to the landmark visualisation task.

63. Maguire EA, Burgess N, Donnett JG, Frackowiak RSJ, Frith CD,
••   O'Keefe J: **Knowing where, and getting there: a human navigation network.** *Science* 1998, **280**:921-924.
A PET study of navigation within a complex virtual reality town. Activation of the right hippocampus was observed when subjects navigated between previously visited locations compared to following a path of arrows. Activation of the right hippocampus and inferior right parietal cortex was correlated with the accuracy of navigation. Interpretation of these results related the hippocampal activity to determining the allocentric direction towards the target, and parietal activation to determining the egocentric turns required to get there.

64. Burgess N, O'Keefe J: **Neuronal computations underlying the firing of place cells and their role in navigation.** *Hippocampus* 1996, **7**:749-762.

65. Maguire EA, Burke T, Phillips J, Staunton H: **Topographical disorientation following unilateral temporal lobe surgery in humans.** *Neuropsychologia* 1996, **34**:993-1001.

66. Farrell MJ: **Topographical disorientation.** *Neurocase* 1996, **2**:509-520.

67. Smith ML, Milner B: **The role of the right hippocampus in the recall of spatial location.** *Neuropsychologia* 1981, **19**:781-793.

68. Bohbot VD, Kalina M, Stepankova K, Spackova N, Petrides M,
••   Nadel N: **Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex.** *Neuropsychologia* 1998, **36**:1217-1238.
A study of patients with well-localised lesions within different areas of the medial temporal lobes, showing that the right parahippocampal cortex is critically involved in topographical memory, as tested by returning to a hidden goal location after a delay (similar to the water maze). The right hippocampus was found to be critically involved in spatial memory, as tested by recall of the locations of objects in a room, and in reproduction of the Rey-Osterrieth figure after a delay.

69. Lepage M, Habib R, Tulving E: **Hippocampal PET activations of**
•   **memory encoding and retrieval: the HIPER model.** *Hippocampus* 1998, **8**:313-322.
A meta-analysis of PET studies showing activation of hippocampal and nearby medial temporal lobe areas during episodic memory encoding or retrieval. The authors observed a tendency for encoding to be associated with anterior hippocampal activations and retrieval to be associated with posterior activations.

70. Schacter DL, Wagner AD: **Medial temporal lobe activations in fMRI**
•   **and PET studies of episodic encoding and retrieval.** *Hippocampus* 1999, **9**:7-24.
Following the LePage *et al.* [69•] paper, this paper presents a similar meta-analysis but includes fMRI studies and reinterprets some of the PET studies differently to Lepage *et al.* [69•]. The authors observe that many fMRI studies, and some PET studies, have shown activation of posterior medial temporal lobe areas associated with encoding. They suggest that the anterior activations in the PET studies described by Lepage *et al.* [69•] might not be attributable to encoding *per se*.

71. Moser M, Moser E, Forrest E, Andersen P, Morris RGM: **Spatial learning with the minislab in the dorsal hippocampus.** *Proc Natl Acad Sci USA* 1995, **92**:9697-9701.

72. Moser MB, Moser EI: **Distributed encoding and retrieval of spatial memory in the hippocampus.** *J Neurosci* 1998, **18**:7535-7542.

73. Hock BJ, Bunsey MD: **Differential effects of dorsal and ventral hippocampal lesions.** *J Neurosci* 1998, **18**:7027-7032.

74. Baxendale SA, Kitchen ND, Thompson PJ, Harkness WF, Shorvon SD: **Postoperative hippocampal remnant shrinkage and memory decline: a dynamic process.** *Epilepsia* 1999, in press.

75. Burgess N, Jeffery KJ, O'Keefe J (Eds): *The Hippocampal and Parietal*
••   *Foundations of Spatial Cognition.* Oxford: Oxford University Press; 1999.
An edited volume of recent research into how the hippocampal and parietal regions of the brain support spatial cognition, either alone or in cooperation. The chapters consider brain damage and functional imaging of the human brain, electrophysiological recording of single neurons in rats and primates, and computer simulation of the action of the networks of neurons. The introduction includes a theoretical framework in which to consider the spatial and mnemonic functions of the two areas.

76. Smith PF: **Vestibular-hippocampal interactions.** *Hippocampus* 1997, **7**:465-471.