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Navigation around London by a taxi driver with bilateral hippocampal lesions

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The time-scale of hippocampal involvement in supporting episodic memory remains a keenly debated topic, with disagreement over whether its role is temporary or permanent. Recently, there has been interest in how navigation by hippocampally-compromised patients in environments learned long ago speaks to this issue. However, identifying patients with damage that is primarily hippocampal, control subjects matched for navigation experience, and testing their *in situ* navigation, present substantial problems. We met these challenges by using a highly accurate and interactive virtual reality simulation of central London (UK) to assess the navigation ability of a licensed London taxi driver who had sustained bilateral hippocampal damage. In this test, patient TT and matched control taxi drivers drove a virtual London taxi along the streets they had first learned 40 years before. We found that the hippocampus is not required for general orientation in the city either in first person or survey perspectives, detailed topographical knowledge of landmarks and their spatial relationships, or even for active navigation along some routes. However, in his navigation TT was very reliant on main artery or 'A' roads, and became lost when navigation depended instead on non-A roads. We conclude that the hippocampus in humans is necessary for facilitating navigation in places learned long ago, particularly where complex large-scale spaces are concerned, and successful navigation requires access to detailed spatial representations.

Keywords: hippocampus; navigation; taxi driver; virtual reality; remote memory

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Introduction

Studies in humans indicate that damage to the hippocampus results in anterograde and retrograde amnesia. Most neuropsychological investigations have focused on examining the neural basis of retrograde amnesia in relation to episodic memory, i.e. recollection of experiences set in their unique spatial and temporal context (*see* Spiers *et al.*, 2001*a*). However, examining the ability to navigate in environments learned long ago is another apposite way to probe remotely acquired memories.

The hippocampus in non-humans is known to be important for navigation since the discovery of place cells, which signal the current allocentric location of the animal in space (O'Keefe and Dostrovsky, 1971). Cognitive map theory posits that these place cells form a cognitive map of a large-scale environment, which persists across the animal's life span, and which is necessary to support flexible navigation, such as taking short-cuts or detours (O'Keefe and Nadel, 1978). Thus, cognitive map theory would predict that flexible navigation in environments learned recently or remotely would be impaired following hippocampal damage.

The data relating to retrograde spatial memory in non-humans, however, are somewhat equivocal. There are reports of preserved remote memory following damage to the hippocampus (e.g. Squire *et al.*, 2005; Winocur *et al.*, 2005*a*), and evidence of disengagement of the hippocampus after initial spatial memory formation (Maviel *et al.*, 2004). In contrast, others have failed to find a temporal gradient in spatial memory following hippocampal lesions, with remote memory impaired in a similar manner to recent memories (Clark *et al.*, 2005*a*, *b*; Martin *et al.*, 2005; Winocur *et al.*, 2005*b*).

There have been several reports about remote spatial memory in patients with hippocampal damage that appear to shed light on this issue. EP became amnesic following extensive damage to his medial and anterior temporal lobes as a result of herpes simplex encephalitis (Teng and Squire, 1999). He had lived in an area of California for 22 years in his early life before moving away. He was tested on his ability to remember aspects of this remotely-learned environment. The tests involved describing routes between home and places in the area, describing routes between different locations (not home), between these locations if a main street was blocked, and imagining being in a particular orientation at certain locations and having to point towards specific landmarks. Compared with five control subjects who had moved away from the area in a similar timeframe, EP was unimpaired. From this the authors concluded that the medial temporal lobes were not the repository of remote spatial memories. Discordant with the cognitive map theory, instead the case of EP is consistent with another theoretical position, the standard model of consolidation, in which the role of the hippocampus in memory (be it spatial or episodic) is regarded as time-limited (Squire and Alvarez, 1995; Squire *et al*., 2001; Bayley *et al*., 2003, 2005).

Another patient, KC, became profoundly amnesic following a closed head injury that caused widespread damage, which included the hippocampi bilaterally, the parahippocampal cortices and infarction to the medial occipital region (Rosenbaum *et al*., 2000). He lived in his small Toronto neighbourhood for 40 years. Compared with four control subjects, KC was unimpaired on a range of topographical memory tests. Specifically he was able to describe routes between places when the most direct route was blocked, indicate directions and distances between landmarks, make proximity judgements between locations, and order landmarks in the sequence they would be passed if one navigated through the area. A similar pattern of performance was reported in another long-time Toronto resident SB, with probable Alzheimer's disease and extensive temporal and occipital damage (Rosenbaum *et al*., 2005*a*). Like Teng and Squire (1999), the authors reject the cognitive map theory, and conclude that the hippocampus is not crucial for the maintenance and retrieval of all remote allocentric spatial representations. However, their overall interpretation differs from Teng and Squire (1999). Rosenbaum *et al.* (2000) and Moscovitch *et al.* (2005, 2006), assert that well-rehearsed spatial layouts may be akin to semantic memories, are devoid of rich topographical detail of the sort that provide the basis for vivid recollection, and therefore independent of the hippocampus but still sufficient to support basic navigation. They argue that the retrieval of detailed perceptual-spatial representations of experienced environments always depend on the hippocampus no matter how long ago they were acquired. They cite the small number of landmarks on KC's sketch map, impoverished detailed geographical knowledge, and impaired ability to recognize incidental landmarks as possible evidence of a deficit in spatial memories formed long ago. This explanation is consistent with the latest formulation of a third theoretical account, the multiple trace theory (MTT), which suggests hippocampal involvement is necessary and permanent for vivid and detailed episodic and spatial memories (Moscovitch *et al*., 2005, 2006).

The evidence from humans, therefore, seems to suggest that even flexible navigation in environments learned long ago is possible without the involvement of the hippocampus. However, there are several issues that arise from these previous studies, which may affect this conclusion. First, there is an obvious tension between the reports of patients KC and SB on the one hand, and that of patient EP on the other. All are apparently unimpaired at navigation, yet in one case (EP) the conclusion is that the hippocampus is not needed for remote spatial memories, while based on the other cases (KC and SB) it is deduced that the hippocampus is implicated in some forms of remote spatial memory. Although, the evidence particularly in KC is suggestive of a possible semantic/episodic distinction in spatial memory, with the hippocampus necessary for the latter, the data are not conclusive. Secondly, based on the three previous cases, the cognitive map theory is rejected, in that all patients seemed able to access allocentric spatial information, and performed well on tasks requiring flexible navigation, such as detours, which are prime indicators of hippocampal-dependent cognitive mapping according to this theory. However, as noted by Rosenbaum *et al.* (2005*a*), environments learned long ago and which are well-practised may have been transformed in the process such that the representations no longer code for allocentric information, being supported instead by brain areas other than the hippocampus. This might be particularly true of environments that have a relatively simple and predictable, regular (grid-like) layout. The neighbourhoods of all of the previous cases, EP, KC and SB, were of this type. Finally, while it is reported that KC navigated normally in his neighbourhood (Moscovitch *et al*., 2005), the third potential concern with the previous patients is the dearth of systematic data relating to their *in situ* navigation ability. While static, or off-line, tests can permit examination of allocentric spatial processing, and are suited to use in memory-impaired patients, additional important information might be gleaned by examining dynamic navigation in the complex real world where it typically takes place.

In order to address these outstanding issues, we investigated what we believe is a unique case. The patient, TT, had damage that was more focal than the previous cases, involving primarily the hippocampus bilaterally (*see* Material and methods). TT had worked for nearly 40 years as a licensed London taxi driver. In the UK, licensed London taxi drivers undergo extensive training over a period of 2–4 years known as 'The Knowledge'. This involves learning the layout of 25 000 streets in the city, thousands of places of interest, leading to a stringent set of examinations by the Public Carriage Office in order to obtain an operating licence. Given TT's occupation, we knew he initially learned London's layout nearly four decades years ago, and had navigated continuously in London since that time. In addition, we knew the standard of his pre-morbid navigation ability, and could compare him with very appropriate control subjects, namely his similarly-qualified and experienced fellow taxi drivers. Unlike the environments of the previous patients EP, KC and SB, London has a high number and density of roads in a very unpredictable and irregular layout, in addition to numerous complex one-way systems. This allowed us to examine the effect of hippocampal damage on navigation in a remotely-learned complex environment where there was an indisputable call on allocentric information. As well as static tests similar to those used in the cases of EP, KC and SB, we expanded on the previous studies by also employing a novel means of assessing *in situ* dynamic navigation. Using a highly accurate and interactive virtual reality rendering of the city of London (UK), we were able to monitor TT and the control taxi drivers as they guided a virtual London taxi along the streets they had first learned 40 years before.

In summary, by examining the unique case of TT, the aim of this study was to determine whether the remotely-formed spatial representation of a complex (irregular layout and high road density) environment, and the ability to actively navigate within it, survived in the context of dense amnesia and bilateral hippocampal damage. As such, we hoped to adjudicate between the three theoretical accounts of the time-scale of hippocampal involvement in remote spatial memory, given that each theory makes a different prediction about TT's performance. If TT was unable to navigate around (virtual) London, this would be support for the cognitive map theory. If he was able to navigate normally, then this would be compelling support for the standard model of consolidation. Finally, if TT was able to navigate in London to some degree, but with a deficit in the finer detail of his spatial representation, this would accord with the MTT.

Material and methods

Participants

Case history

TT was a 65-year-old-right-handed man who left school aged 15-years-old. He completed his National Service then worked as a tailor, and for the last 37 years as a licensed London taxi driver. He stopped working 2 years prior to our investigations, at the onset of his illness. TT, being previously healthy, presented with a 6 weeks history of rapidly progressive amnesia and confusion, 2 weeks after a diarrhoeal illness. He was noted to keep asking the same questions, and frequently got lost. Four months later, he had a series of complex partial and tonic-clonic seizures. After extensive clinical investigations, it was established that TT had limbic encephalitis associated with voltage gated potassium channel antibodies (VGKC-Ab; Vincent *et al.*, 2004). This rare and quite recently described condition is often paraneoplastic, but extensive examinations of TT did not reveal any malignancies. TT was administered a range of therapies, including plasma exchange, that did not improve his memory deficits. He was then placed on a corticosteroid regimen that improved his attention, concentration and the general clarity of his thinking, although his memory remained very impaired. TT participated in the current research some time after the corticosteroids were introduced, and was maintained on the same dose throughout our investigations. Also at this time his VGKC-Ab levels were negative (i.e. normal), and he underwent an MRI brain scan (Fig. 1). This showed damage

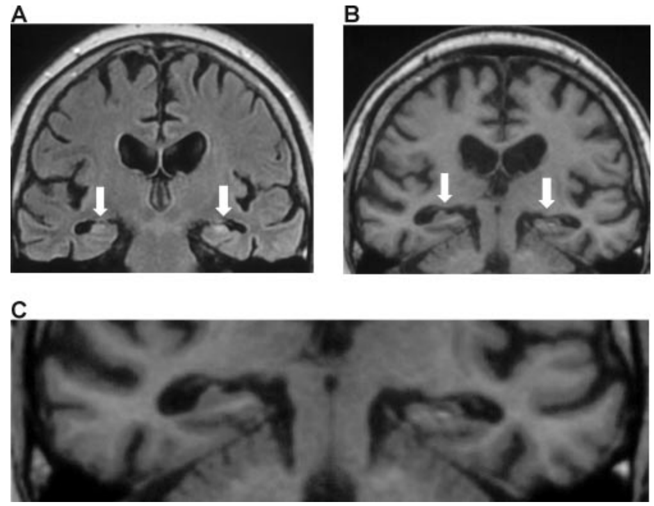

Fig. 1 Coronal sections from the patient's structural MRI scan, with the white arrows indicating the atrophic hippocampi (see Methods for more details). (**A**) FLAIR image from a section through the anterior temporal lobes. (**B**) A T_1 image from a more posterior section. (**C**) A magnified view of TT's medial temporal lobes taken from his T_1 structural scan.

throughout the length of both hippocampi. There was some generalized atrophy, but in this context, entorhinal, perirhinal and parahippocampal cortices appeared intact, as did the mamillary bodies, fornix and thalamic nuclei.

When attempting to deduce the functions of a particular brain area, ideally the patient's damage should be selective to that brain region. However, even exacting measurements of tissue volumes from patients' MRI scans cannot provide a definitive answer as to whether, *in vivo*, that tissue is functioning or not, or to what extent, how it interacts with neighbouring tissue, or the functional effect of a lesion on adjacent and wider brain systems. Thus, one could measure tissue volumes in TT, but this would still not allow us to make any unequivocal claims about the true selectivity of his lesions or allay fears about possible hidden damage either in the medial temporal lobes or elsewhere in the brain. In a single case, such as TT, we instead advocate an approach of lesion description from high-resolution MRI scans, combined with detailed neuropsychological [and where possible functional MRI (fMRI) evidence] to make common sense conclusions about whether a lesion seems to involve a particular brain area. On this basis, we do not claim TT's hippocampal lesions are 'selective', rather instead, we observe that TT's lesions appear to implicate primarily the hippocampi. Notwithstanding the difficulties inherent in this field, we feel that the case of TT permits conclusions to be drawn regarding the hippocampus (see Discussion for more on this).

TT was evaluated with a battery of neuropsychological tests (Table 1). His verbal and performance IQs were borderline average, in line with the estimate of his pre-morbid intellectual functioning. He performed normally on a wide range of tests including those assessing executive, perceptual and language functions. In contrast, he had a severe impairment of anterograde memory, encompassing recognition and recall, in the visual, topographical and verbal domains. He also had profound retrograde memory loss for

Table 1 Neuropsychological profile of patient TT

Test	Score
Wechsler Abbreviated Scale of Intelligence (WASI)	
Full scale IQ	88 (low average)
Verbal IQ	88 (low average)
Performance IQ	91 (average)
Wechsler Test of Adult Reading (WTAR)	
Estimated pre-morbid full scale IQ	90 (average)
Boston Naming Test (short form, /15)	12
The pyramids and palm trees test (/52)	50
Wechsler Adult Intelligence Scale-Revised (WAIS-R)	
Digit span (scaled score)	7
Wechsler Memory Scale III (WMS-III)	
Spatial span (scaled score)	4[a]
Cognitive estimates test	50th percentile
Weigl's test	Passed
Trail Making test[b]	
A	0 errors; 86″
B	1 error; 159″
Verbal fluency (scaled score)	8
Visual Object Space Perception (VOSP) battery	
Incomplete letters (/20)	20
Object decision (/20)	20
Dot counting(/10)	10
Position discrimination (/20)	20
Number location (/10)	8
Cube analysis (/10)	9
Benton visual form discrimination test	31
Benton facial recognition test	49
Benton judgement of line orientation	23
Benton left-right orientation test	18
Recognition of famous faces[c] (/30; taxi control mean 25.3, SD 2.16)	26.5
Warrington recognition memory test	
Words (/50)	27[a]
Faces (/50)	36[a]
Wechsler Memory Scale-Revised (WMS-R) logical memory	
Immediate recall	65th percentile
Delayed recall	1st percentile[a]
Rey – Osterrieth complex figure	
Copy (/36)	35
Delayed recall (30 min, /36)	8[a]
Autobiographical memory interview (AMI)	
Autobiographical	
Childhood (/9)	0[a]
Early adult life (/9)	0[a]
Recent life (/9)	0[a]
Personal semantics	
Childhood (/21)	21
Early adult life (/21)	21
Recent Life (/21)	10[a]
Memory for public events[d] (/35; taxi control mean 28, SD 1.63)	12[a]
Benton visual retention test, version A	5
Doors and people test	
Overall age-scaled score	3[a]
Visual memory age-scaled score	5[a]
Verbal memory age-scaled score	4[a]
Recall age-scaled score	4[a]
Recognition age-scaled score	5[a]
The Camden memory tests	
Paired associate learning	$T_1 = 5^a$; $T_2 = 10^a$
Short recognition memory test words (/25)	19[a]
Short recognition memory test faces (/25)	22
Unfamiliar landscapes recognition memory test (/50)[e]	35[a]
Unfamiliar buildings recognition memory test (/50)[e]	36[a]
Easy building recognition memory test (/25)[f]	21[a]
Wechsler Intelligence Scale for Children-III (WISC-III): mazes sub-test	Passed
Money road map test of direction sense	8 errors
Spatial rotation flags test (abbreviated version) (/42)	36

[a]Impaired.
[b]TT was accurate but slow in psychomotor tasks, experiencing some shaking of his hands, thus slowing his times.
[c]A famous faces test was constructed for this study, and the retired taxi driver control subjects were also tested. Scoring was 1 point for correct name and information (e.g. occupation) and 0.5 for correct identifying information but no name. The items TT got incorrect were people who had come to particular prominence approximately in the last 3 years
[d]A public events test was constructed for this study, and the retired taxi driver control subjects were also tested. Seven decades were examined, with five events (photographs) per decade. A score of 1 point was awarded per event only if the year (+/− 3 years), location, and clear details of what occurred were provided. Of the 12 items TT recollected, two were within the last 3 years (9/11; capture of Saddam Hussain).
[e]Details of these tests and normative data for elderly subjects are reported in Cipolotti and Maguire (2003).
[f]Details of this test and normative data for elderly subjects are reported in Clegg and Warrington (1994).

autobiographical event memories and public event memories extending back over 60 years. TT's ungraded retrograde amnesia might be regarded by some as evidence of extra-hippocampal damage. However, this notion is the subject of heated debate in the literature (see most recently Cipolotti and Moscovitch, 2005 versus Squire and Bayley, 2006). In fact, given that EP and KC also had very extensive retrograde amnesia for episodic memories, a similar pattern in TT means that any findings in TT that differ from the previous cases cannot be attributed to differences in retrograde episodic memory.

Control subjects

Ten male control subjects participated, one was left-handed. All were neurologically and psychiatrically healthy. Their mean age was 71 years (SD 3.63), and on average they left school aged 14-years-old (SD 0.32). The mean estimated full scale IQ of the control group was 98 (SD 6.52). The control subjects were also licensed London taxi drivers and on average had 41 years (SD 12.9) taxi driving experience. Seven of the control taxi drivers retired around the same time TT had become ill (mean 2.64 years ago), and two had drastically cut back on their working hours around that time, such that they worked <2 days per week. The final control subject retired from taxi driving 19 years ago. Across all tests, there was no significant difference between the seven fully retired taxi drivers and the two part-timers, or between the long-time retired individual and the other controls. Thus, hereafter control subjects are treated as one group. There were no significant differences between TT and the control group in terms of age [$t(9) = -1.58$, $P = 0.15$]; years experience as a licensed London taxi driver [$t(9) = -0.3$, $P = 0.77$]; time since retirement [$t(8) = -0.27$, $P = 0.8$, excluding the long-retired individual] and IQ [$t(9) = -1.17$, $P = 0.27$].

The patient (and his spouse) and all control subjects gave informed written consent to participate in the study in accordance with the local research ethics committee. All subjects were video game naïve.

Stimuli

Static topographical memory tests

All photographic stimuli were of a similar high quality and high-resolution, colour, taken at eye level, and of a uniform size (21 × 14.6 cm).

London landmarks recognition memory test. Given that licensed London taxi drivers would be expected to perform very well on tests of London landmarks, we aimed to increase the difficulty of the test (and avoid ceiling effects) by using distractor landmarks that were highly visually similar to the London landmarks. In the case of all photographs, electronic alterations were made to exclude background cues to their whereabouts. During the test, subjects were shown 48 colour pictures of landmarks one after another. Half of the pictures were of famous London landmarks and half were the distractor landmarks that were neither famous nor in London. The target and distractor landmarks were randomly intermixed. The test format was a yes/no recognition test where subjects were asked to state whether they recognized each landmark as a famous London landmark or not. The test was not formally timed however; subjects on average took about 5 s per photograph. A similar procedure was followed for the World landmarks recognition memory test.

London landmarks proximity judgements. Stimuli were in the form of colour photographs, each depicting one London landmark. Subjects were required to judge which of two London landmarks was closer (as the crow flies) to a third London landmark. There were 10 trials.

London landmark distance judgements. Subjects were shown two photographs of famous London landmarks and were required to estimate the absolute distance between the landmarks (as the crow flies). They could give their answers in metric or imperial measurements (all subjects used imperial). There were five trials. The estimated distance was expressed as a percentage of the correct distance measurement.

London landmark location on a map. Subjects were presented with an A3 sized (297 × 420 mm) skeleton road map of central London, taken from an ordinance survey map of the same size. Only the main roads, two of the main parks, and the River Thames were represented. Subjects were asked to mark on the map where they believed a series of 15 significant landmarks were located. The landmarks were shown as typewritten words, one at a time. For each landmark the maximum locational accuracy score was three points. This was achieved if placement was within 1 cm (211 m) of the true location of the landmark, or within the boundary perimeter of the landmark area as detailed on the master map. Two points were awarded if placement was within 2 cm (422 m) of the correct location and on the correct side of the road. One point was awarded if the map placement was within the correct general area of the actual place, but outside of the 1 or 2 cm range.

Direction sense. This test took place in a large room on the 4th floor of the department with a window running along the length of the north east wall. Each subject's initial orientation was verified by asking them point to the nearby hospital opposite the department. At the start of each trial the subject was repositioned at the same start location in the room. He was given a device comprising a long plastic handle, at the end of which was a compass. The compass was obscured from the subject's view by means of a cardboard screen attached to the plastic handle. A location was given verbally by the examiner and the subject had to point to the location using the compass device as an extension of his arm. The locations were all across London in all directions and varying distances, none of which were visible from the subject's position. Once the subject was happy with his response, the examiner read off the compass bearing and then repositioned the subject ready for the next trial. There were 12 trials in total. The subject's pointing direction was compared with the correct direction for each landmark and a percentage deviance from the correct angle determined. The correct direction was computed from map position data for each of the locations and a correction for the difference between magnetic north and grid north.

Active navigation

Virtual reality London. The video game 'The Getaway' (© Sony Computer Entertainment Europe 2002) run on a Sony Playstation2 (© Sony Computer Games Inc) was used to present subjects with a ground-level first person perspective view of a simulation of central London. The game designers decided to truly recreate the city and a large team of photographers walked the streets of central London for 2 years recording many streets, shops and other details. Over 110 km (70 miles) of driveable roads have been accurately recreated from ordinance survey map data, covering 50 km^2 (20 square miles) of the city centre. The one-way systems, working traffic lights, the busy London traffic and an abundance of Londoners going about their business are all included. The area covered in the game stretches from Hyde Park in the west to Shoreditch and Bethnal Green in the east; from the Angel in the north to Lambeth Bridge in the south. There are no readable street signs in the game, so one has to rely on extant knowledge to navigate. Breaking all speed limits and ignoring all red traffic lights, it takes 15 min to travel between the furthest points east to west. Conveniently, one can simply drive freely around the city using the game console, with a normal ground-level first person perspective, in a car of one's choice, in our case a London taxi. See Fig. 2 for still images from the environment (*see* also Spiers and Maguire, 2006, for additional details of the virtual reality London). Crucially, the realistic nature of the environment, with one-way systems and traffic restrictions, embodies the need to be able to take detours and short-cuts. Also of note, the game was developed ~4 years prior to our study. Thus, the London captured in the game is London as it was ~2 years before TT became ill. This is important because it allowed us to test TT in the London that he experienced, and without changes to buildings or layout that may have occurred since (or in the 2 years

Fig. 2 Example views from within the video game 'The Getaway' © 2002 Sony Computer Entertainment Europe. Upper panel shows a view at Trafalgar Square, middle panel a view at Piccadilly Circus, lower panel a view looking towards the London Eye/Millenium Wheel. These images are reproduced with the kind permission of Sony Computer Entertainment Europe.

before) he stopped taxi driving. All of the taxi drivers confirmed that the game was very reminiscent of their experience of navigating in central London. One moves through the environment by controlling a virtual taxi cab using a game controller, consisting of two joysticks providing analogue control of acceleration, braking and steering left and right. Pilot work indicated that elderly subjects who are video game naïve have difficulty learning to use the game controller, and this distracts from the navigation experience. Thus, in the study the game controller was operated by H.J.S. Crucially, the 'driver' made no navigationally-relevant decisions whatsoever, with all his movements guided throughout by the subjects. They were instructed to navigate 'legally' as they would in actual London, observing all traffic restrictions and one-way systems. The 'Free Roaming' mode of the game was used, permitting free navigation with the normal game scenarios suspended. To avoid collisions with other vehicles in the environment, Action Replay Max software (© Datel Design and Development Ltd 2003) provided a 'cheat' modification to the game, permitting one to drive through other vehicles.

Virtual reality navigation test. Subjects' navigation was tested by picking up customers at start points in the city, and taking them to specified destinations. Our main criteria in designing the test was to have likely, legal routes that sampled widely across central London, with minimum overlap between routes, and minimal effects of the game (i.e. we avoided those areas where streets were not rendered in as much detail, or where streets were missing in the game). Navigation performance was measured in terms of the distance error. Based on a pilot study involving a different group of licensed London taxi drivers, consistently-chosen legal routes were established for each trial, and the ideal minimum length of these routes was computed. The distance each subject drove on each route and the ideal distance for each route were measured using Map24(UK) (http://www.uk.map24.com). The deviance from these likely routes was calculated as the percentage distance error (i.e. the amount of extra distance travelled compared with the ideal distance; Spiers *et al.*, 2001*b*). An additional measure, a disorientation score (the number of times a subject appeared obviously disoriented) was included in the initial plan for the study because we were concerned that qualitative aspects of performance en route might not be reflected in the overall distance error score. However, this was not the case and in fact, as one might expect, the two measures were correlated. Route variables (e.g. % non-A roads) were highly similar for both the game and the real world, given that one of our criteria in route selection was to minimize the effects of the game and use areas of London rendered most realistically. Thirteen routes were tested. These are listed on Table 3.

Data analysis

Data were analysed using standard statistics (*t*-tests, ANOVA and χ^2). All results are two-tailed with a significance threshold of $P < 0.05$. Of note, where the patient was compared with the control group, a modified *t*-test was used (Crawford and Howell, 1998; Crawford and Garthwaite, 2002). This test treats an individual patient as a sample, affording the comparison of the patient and a reasonably small control group. The extraction method for the factor analysis was a principal components analysis. The rotation method was varimax with Kaiser normalization.

Table 2 Performance on static topographical tests

Test	TT	Control mean (SD)
London landmark recognition (/48)[a]	36	38.4 (5.13)
World landmark recognition (/48)[a]	40	37.3 (3.3)
London landmark proximity judgements (/10)	8	9 (0.67)
London landmark distance judgments (mean % deviation from correct)	194	114 (66.63)
London landmark location on a map (/45)	28	21.9 (11.12)
Pointing to places in London[b] (mean % deviation from correct location)	4.6	5.5 (2.87)

Note that TT also performed with a mean (across 10 trials) 4.6% deviance error in another vector mapping test. Similar to the test used by Rosenbaum *et al.* (2000), TT was presented on each trial with a sheet of paper with only the north and south borders of central London shown, and the location of one landmark. He was required to draw an arrow indicating the correct direction from this landmark to another verbally given landmark.
[a]Note that our efforts to prevent ceiling effects in this group of London experts by devising landmark tests with a high degree of difficulty was successful, with control subjects scoring on average 80% correct.
[b]See Fig. 3 for the raw scores for each subject for each location.

Results

Static topographical memory tests

In the first instance a range of topographical memory tests were administered to TT and the retired taxi drivers, designed to assess various aspects of London landmark knowledge and their spatial relationships (*see* Material and methods for further details). Administration of these static tests also afforded the opportunity for comparison with previous patients, such as EP (Teng and Squire, 1999) and KC (Rosenbaum *et al.*, 2000), whose testing was of this type. TT's performance and the means for the control group are given in Table 2.

Landmarks

The consistent result across the static tests was that TT performed at a comparable level to control subjects. Specifically, there was no significant difference between TT and the control group in the ability to recognize famous London landmarks [$t(9) = -0.446$, $P = 0.67$]. In a separate testing session, TT was asked to call certain London landmarks to mind and describe them. He was able to provide detailed descriptions of their physical appearance (e.g. colours, shapes, textures, building materials, number and types of windows), general knowledge about the landmarks, the areas of London in which they are located, and descriptions of activities that take place in there. TT's ability to discriminate between visually complex stimuli was not just confined to London landmarks. There was no significant difference between TT and the control group in his ability to discriminate and recognize famous world landmarks from among visually similar foil landmarks [$t(9) = 0.78$, $P = 0.46$].

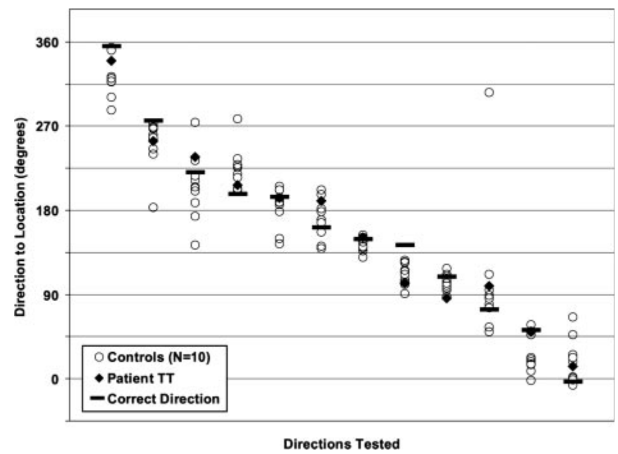

Fig. 3 Performance on the direction-pointing task. Subjects were asked to point to different places in London from a fixed location in the laboratory (see Material and methods). Responses were compared with the correct direction relative to magnetic north for each of 12 locations. The data for every location for each subject and patient TT are shown in descending order rather than the order tested. Note, these are circular data shown in flattened format for ease of viewing.

Spatial relationships

Beyond landmark recognition, it is important to know the relationships between landmarks as a basis for a viable spatial represenation of an environment. TT's knowledge of the proximal relations between landmarks was intact, with no difference between his performance and that of the control group [$t(9) = -1.423$, $P = 0.19$]. Similarly, his ability to estimate absolute distances did not differ from control subjects [$t(9) = 1.14$, $P = 0.28$]. We next tested subjects' knowledge of London from an aerial or survey perspective. Given a skeleton road map of central London (main roads only and no street names) subjects had to mark on the map the location of given landmarks. As before there was no significant difference between TT's performance on this test and that of the control group [$t(9) = 0.523$, $P = 0.61$]. Another key component of navigation is being oriented, knowing the direction of locations relative to your current position. Subjects were asked to point to different places in London from a fixed location in the laboratory. Subjects' responses were recorded and compared with the correct direction for each location. There was no significant difference between TT's mean percentage deviance from the correct directions and that of the control group [$t(9) = -0.285$, $P = 0.78$]. Fig. 3 shows the raw scores of each subject for each location on this test. It serves to underline just how accurate TT's direction sense was for places in London.

Sketch maps

Normally when one assesses topographical knowledge of an environment, it is usual to ask subjects to draw a sketch map of the roads and salient landmarks. We asked the control taxi drivers to provide a sketch map. Given that they know

25 000 streets, they found this request very difficult to comply with and we were faced with a test that effectively had no end. Even when asked to restrict their map to one small area, they had so much knowledge of the fine detail of the streets that the same problem occurred. When TT was asked to provide a sketch map, he had exactly the same reaction as the control taxi drivers, finding this request very hard to understand and, like them, was unable to comply. Instead, we focused on TT's ability to provide sketch maps on a much smaller scale, namely the basic floor plan of his home. Prior to his illness, TT and his wife had lived in the same house in London for 36 years. After he recovered from the acute phase of his illness, they moved to a smaller apartment in a suburb just outside central London. His floor plans for pre- and post-lesion homes were inaccurate compared with his wife's, although not grossly impaired. In both cases, he mis-located some key features, for example in the pre-lesion house, he put the main staircase in the incorrect place, in the post-lesion apartment balconies were associated with the incorrect rooms.

In summary, it is clear that TT, despite his profound memory impairments, retains a striking amount of navigationally-relevant information. In particular, he seems to have normal landmark, relational and orientation knowledge about central London, an area he navigated in everyday for nearly 40 years. Nevertheless, the question remained, even with a wealth of knowledge at his disposal, would his ability to actively navigate also be preserved?

Table 3 Active navigation in (virtual) London: percentage distance error*

Route†	TT	Control mean (SD)
1. Piccadilly Circus to Big Ben	0	2.4 (7.59)
2. Big Ben to Horse Guards Parade	0	4.7 (4.45)
3. Broadwick Street to Berwick Street	0	19.7 (32.06)
4. Horse Guards Parade to Glasshouse Street	0	5.4 (11.42)
5. Kings Cross Station to the British Museum	0	22.9 (9.12)
6. Middlesex Hospital to Kings Cross Station	0	0 (0)
7. Holborn tube station to St Paul's Cathedral	12	0 (0)
8. Holborn tube station to the River Thames	16	4.9 (8.44)
9. Berkeley Square to Berwick Street	69	24.5 (21.81)
10. Glasshouse Street to Berkeley Square	86	20 (26.14)
11. St Paul's Cathedral to the Bank of England	100§	0 (0)
12. Berwick Street to Golden Square	100	7.1 (22.45)
13. The British museum to St Paul's Cathedral	100	23.3 (20.34)

*See also Fig. 4 for the data for each subject for each route; †NB routes were not performed in the above order; routes are presented in this order on the above table and in Figs 4 and 5 to better illustrate the pattern of TT's performance; §Where percentage distance error is 100%, this means the destination was not reached despite protracted efforts.

Active navigation

Learning a new environment

First we inquired whether TT was able to learn to navigate in a new environment unknown before his illness. As mentioned above, TT and his wife moved to a suburb just outside central London after his illness. His wife reports that despite covering the same routes through the neighbourhood and around the local shopping centre many times, TT has been unable to learn to find his way, and cannot navigate independently. This inability to acquire a new spatial representation is in line with his general anterograde memory impairment, and similar to anterograde spatial memory deficits in patient KC and others (Rosenbaum *et al.*, 2000; Burgess *et al.*, 2002).

Navigating in an environment learned long ago: central London

We next assessed TT's ability to navigate in central London, to see if he could put his wealth of preserved knowledge, as assessed on the static tests reported above, to good use. Subjects' navigation was tested in virtual reality London by picking up customers at start points in the city, and taking them to specified destinations. The deviance from the ideal routes was calculated as the percentage distance error (i.e. the amount of extra distance travelled compared with the ideal distance—*see* Material and methods). Of note, there was a high degree of consistency in the routes chosen across the control subjects, and this accorded well with the routes identified in the pilot study. Considering the mean percentage distance error across routes, overall TT's routes were significantly longer than the control subjects [$t(9) = 2.56$, $P = 0.03$].

One might conclude from this that TT's *in situ* navigation in London was generally impaired, and navigation using a spatial representation formed long ago does in fact require the integrity of the hippocampi. However, examination of Table 3 and Fig. 4A shows that there was a clear dichotomy in TT's performance. For half the routes, TT navigated perfectly, for the other half of the routes he deviated from the ideal routes, and in the case of five of those routes, to a large extent, often not able to reach the destinations (*see* also Fig. 4B). Considering only those routes where TT was errorful and comparing his performance with that of the control subjects on the same routes, TT was significantly worse than the controls [$t(9) = 5.06$, $P = 0.001$].

Why could TT navigate along some routes but not others?

We did not design the set of routes with any dichotomy in mind (*see* Material and methods). Having observed the stark

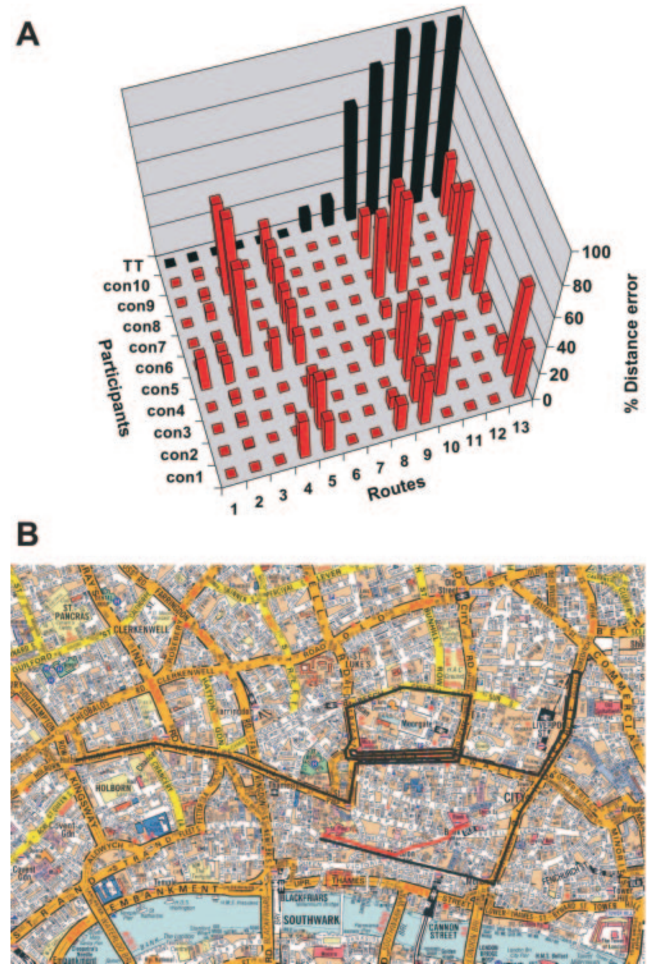

Fig. 4 Navigation performance. (**A**) A 3D graph showing navigation performance around (virtual) London for each route for every subject (see text, and Table 3). Note: routes were not performed in the order shown but are presented in this way, and in Table 3 and Fig. 5, to better illustrate the pattern of TT's performance. (**B**) An example of navigation performance for Route 11 (St Paul's Cathedral to the Bank of England). All 10 control subjects performed in an identical manner, shown in red on this map. TT was grossly impaired; his route is shown in black. Map reproduced by permission of Geographers' A–Z Map Co. Ltd © Crown Copyright 2005. All rights reserved. Licence number 100017302.

dichotomy in TT's navigation performance apparent in Table 3 and Fig. 4, we naturally wondered what might differ between the two kinds of routes, those on which he was errorfree and those where he was errorful. We now outline a series of additional analyses where we considered a number of variables that might have influenced the findings.

One might wonder if the routes where TT was errorful were somehow more difficult even for the controls. However, comparison of the controls' performance on the routes where TT made errors with their performance on the routes where TT was errorfree, showed no significant difference between the two route types [$t(11) = -0.39$, $P = 0.71$]. We next verified that TT's performance was not somehow affected by difficulty in perceiving and recognizing landmarks as rendered in the game, even though they are depicted very well. This was not the case, as in a recognition test TT correctly identified 13/15 landmark pictures from the game (of note, the 2 he did not recognize are landmarks not normally accessible by cars, thus TT was unlikely to have seen them unless he visited on foot). We also established that the pattern of performance was not due to a basic failure by TT to remember his destination during the errorful routes, as he mentioned the destination at points along each of the routes during the navigation test. Neither was it the case that the order of the routes influenced his performance. Moreover, TT was not more errorful as the testing session progressed, and within errorful routes the proportion of the total errors that occurred at the start, middle and towards the end of routes did not differ significantly [$F(2,18) = 0.66$, $P = 0.53$].

We next considered if TT's errorful routes were somehow less frequently used by taxi drivers. After the navigation test, we asked subjects to rate how frequently they used the routes they chose between the start and destination points. As with the sketch map, the subjects (controls and TT) found this a very hard question to comprehend. With on average 40 years experience of taxi driving in London, they felt they had 'done it all' so many times that no roads in central London were more or less frequently used. Nevertheless, we persuaded them to give a rating for each route on a 5 point scale (5 = very frequently used . . . 1 = very infrequent). There was no significant difference between TT's average rating and those of the controls [$t(9) = -0.68$, $P = 0.51$], or in the overall pattern of ratings across the routes for TT and controls.

It could be argued that, compared with static tests, the virtual reality task, with trials over several minutes, might have been adversely affected by TT's anterograde memory deficit. However, the navigation routes which elicited impairment in TT did not take any more time than those where he was errorfree, did not involve more turns, or more decisions. At no point did TT forget what he was doing or get distracted. Nevertheless, to probe this in more detail, we employed an additional set of tests, which were less complex, and considerably shorter in the time required for each trial. We got TT to verbally describe routes. On the advice of taxi drivers, we devised a test of eight common routes that they would regularly take in central London. TT was asked to describe getting from start to end point. He was very impaired on this test, scoring only 2/8. In a separate session, we asked him to verbally describe the routes where he navigated without error during the VR navigation test. Here again, TT was very impaired to the degree that the test had to be terminated after four routes because TT got very frustrated and had to give up on every route, including a route that was one of the shortest and simplest. In this test, a common error appeared to involve TT missing out turns onto streets that would have been appropriate to use. These findings suggest that the VR navigation test, rather than causing problems for TT, actually helped him, probably by

Table 4 Virtual London navigation test: route variables and factor analysis

For each route	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
TT % distance error	*					
TT disoriented at some point	*					
Control mean % distance error				*		
Controls' ratings of route frequency			*			
No. of times TT forgot destination					*	
TT's initial route decision good						*
TT used roads the controls didn't	*					
Length of ideal (legal) route						
Direct length (i.e. as the crow flies)		*	*			
More wide than narrow roads						
No. of detours to be made on the ideal route					*	
No. of decision points		*				
No. of decision turns		*				
No. of possible viable options				*		
No. of roundabouts/squares						
No. of major landmarks						
Degree of visual detail[a]						
No. of roads		*				
No. of one-way roads						*
No. of one-way roads causing detours		*				
No. of A roads						
No. of non-A roads	*					
High non-A road density around the route	*					
Overall road density around the route	*					
No. of different routes chosen by controls				*		
Facing in opposite direction at start point						
Must drive away from destination initially						
Route going mainly in one direction						*
Order routes were attempted			*			
Occasional lack of detail in the game					*	

See main text of Results section for further analysis of Factor 1.
Factor 5, with the variable 'Number of times TT forgot destination', might be perceived as also being performance–relevant. However, this variable did not distinguish between the two route groups [$t(11) = -1.13$, $P = 0.28$] nor did its fellow Factor 5 variables 'Numbers of detours to be made in the ideal route' [$t(11) = -0.62$, $P = 0.55$], 'Occasional lack of detail in the game' [$t(11) = -0.24$, $P = 0.82$].
Factor 7 accounted for just 6.4% and so is not included in the table.
[a]Using a 10 point rating scale, each route was rated (by HJS) according to the overall number and distribution of landmarks/features (10 = very visually detailed).

providing constant visual cues to his whereabouts as well as possible route and turn options. Thus, while TT's anterograde memory deficits are pertinent to consider, we maintain the evidence summarized above speaks against a simple anterograde memory explanation for the dichotomous results.

Route characteristics: factor analysis

Having ruled out a number of variables as explaining the findings, we proceeded to interrogate the striking dichotomy in TT's VR navigation performance further by analysing each route along 27 different parameters. These included basic variables, such as numbers of decision points and turns, length and presence of landmarks. Including the navigation performance of TT and the controls, a factor analysis was then performed on the route variables in order to generate some potential causal mechanisms underlying TT's navigation pattern. The route variables and the results of the factor analysis are shown on Table 4. Seven factors were identified as explaining 93.06% of the variance. Factor 1 = 27.82%; Factor 2 = 15.01%; Factor 3 = 14.97%; Factor 4 = 10.56%; Factor 5 = 9.6%; Factor 6 = 8.7% and Factor 7 = 6.4%. Factor 1 explains the largest amount of variance, and interestingly includes TT's distance error. Four other route variables are grouped with TT's performance scores in Factor 1: the number of non-A roads on routes, a high density of non-A roads in the vicinity of routes, the overall road density in the vicinity of routes, and TT's use of roads that the control subjects didn't use. In the UK, main artery roads are called A and B roads. On the London map in Fig. 4B, these are the prominent orange (A roads) and yellow (B roads) coloured roads. Here we classed both types of main road under the heading of A roads.

'A' versus 'non-A' roads

We took the routes and divided them into two groups, those where TT was errorful and those where he had been errorfree. Having identified the variables (Factor 1) that

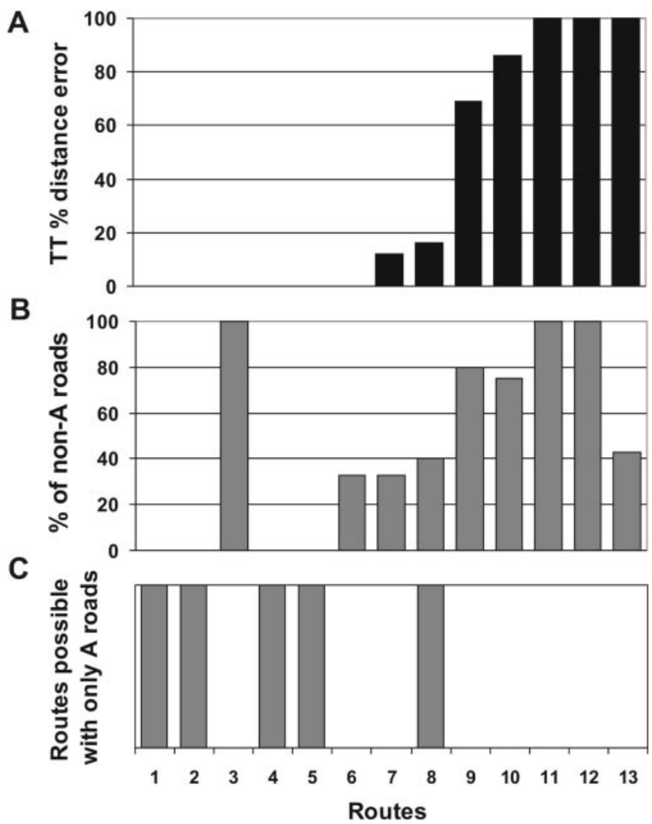

Fig. 5 Non-A roads. The top panel (**A**) reprises TT's navigation data across the 13 routes (see also Fig. 4A and Table 3). The middle panel (**B**) shows the corresponding percentage of non-A roads for each route. The bottom panel (**C**) indicates whether routes could be navigated using only A roads. See text for further details of Route 3 (Soho).

might be related to TT's navigation performance, we then compared the two sets of routes on each of these variables. The two types of route did not differ significantly in terms of TT's usage of streets the control subjects didn't use (χ^2 = 0.619, P = 1), or in terms of the high density of non-A roads in the vicinity of routes [$t(11) = -1.51$, $P = 0.16$). However, the two route groups did differ significantly for overall road density in the vicinity of routes [$t(11) = -2.32$, $P = 0.04$] and the number of non-A roads on routes [$t(11) = -3.92$, $P = 0.002$] where TT's errorful routes had a greater road density in the vicinity of the routes, and a higher number of non-A roads on the routes. As this factor analysis was exploratory and to reduce the chance of Type I error, Bonferroni correction ($P = 0.0125$) was applied leaving one variable as significant, namely, the number of non-A roads on the routes. Fig. 5 shows TT's distance error across routes, along with the non-A roads on routes, and also a breakdown of routes according to whether the route could be navigated using only A roads. It is clear that where routes lacked A roads, or could not be navigated primarily using A roads, then TT's performance was adversely affected.

Thus, had we confined our tests to static topographical stimuli, we would have pronounced TT unimpaired. However, by testing active *in situ* navigation in a complex environment, and engaging in a detailed analysis of factors underlying the routes used, a much more informative picture has emerged of TT's navigation ability, and the role of the hippocampus in navigation and remote spatial memory.

Discussion

We described the case of licensed London taxi driver TT, who learned the layout of London nearly 40 years ago, and had navigated in the city ever since. We tested the status of his navigation ability in the context of acquired bilateral hippocampal lesions and amnesia. Our results showed that the hippocampus is not necessary for general orientation in London, rich and detailed topographical knowledge of landmarks, and the spatial relationships between them, or even for navigation along some routes. However, TT was extremely reliant on using main artery, or A, roads to navigate, and became lost when the use of non-A roads was required. This suggests the hippocampus is crucial for navigation in environments learned in the very remote past, and specifically houses or accesses the fine-grained and detailed spatial representation of a city's layout.

TT has much in common with the previously reported cases EP (Teng and Squire, 1999), KC (Rosenbaum *et al.*, 2000) and SB (Rosenbaum *et al.*, 2005*a*), and his case is further confirmation that an impressive amount of navigationally-relevant information is retained in the face of bilateral hippocampal damage. Where TT differs from the other cases is in the ability to actively navigate in his environment, which is not wholly preserved. What might the reason be for this distinction between TT and the other patients? We consider three possibilities.

First, TT's damage is more focal than in the other cases, involving primarily the hippocampi. It is unlikely, however, that his greater impairment resulted from more circumscribed lesions. Secondly, TT's deficit was revealed by the use of dynamic tests of *in situ* navigation, while the conclusions about the status of remote memory in EP, KC, and SB were made based on the static testing. It could be that dynamic testing is somehow more sensitive to the integrity of spatial representations of large-scale space. The finding of preserved A road and impaired non-A road navigation in TT would have been difficult to discover using static tests. However, patient KC was reported to be able to navigate unaided in his neighbourhood (Moscovitch *et al.*, 2005), and the static tests employed in KC in particular were challenging and might have been expected to elicit a navigation deficit if one existed. Alternatively, it could be that the dynamic tests placed much greater demands on anterograde memory and this is why TT, with anterograde amnesia, registered a deficit on these as opposed to the static tests. The circumstances under which one might expect this would be where navigation occurs over several minutes or longer, and involves multiple turns and decisions (Knowlton and Fanselow, 1998; Clark *et al.*, 2005*a*). However, the navigation routes, which elicited impairment in TT did not take any more time than those where he was errorfree, did not involve more turns or more decisions. At no point did TT forget what he was doing or get distracted, and he rarely forgot the destination, and not moreso for the errorful routes. Moreover, the verbal route description tests were considerably shorter in terms of time required on each trial, yet TT was still impaired. Therefore, we conclude that static and dynamic tests complement each other, and this factor is unlikely to explain the distinct findings in TT.

The third way in which TT and the other cases differ is in terms of the nature of the environment that was learned long ago. Unlike the environments of the previous patients EP, KC and SB, London has a high number and density of roads in a very unpredictable and irregular layout, in addition to complex and numerous one-way systems. It may be that one or a combination of these features requires functioning hippocampi, whereas for the environments of the other patients, particularly when highly familiar, the hippocampal role is minimized. In the previous cases, and for the information retained by TT, other brain areas such as parahippocampal, parietal and retrosplenial cortices and striatum may have been sufficient (Maguire, 2001; Burgess *et al.*, 2002; Hartley *et al.*, 2003; Iaria *et al.*, 2003). That the nature of a large-scale space is vital to consider in questions about hippocampal involvement is further supported by several fMRI studies. Rosenbaum *et al.* (2004) had subjects perform a number of topographical memory tasks based in the downtown area of Toronto (the city of patients KC and SB). This included a task where subjects imagined navigating and taking detours. The hippocampus was not activated above baseline in any of their Toronto-based tasks. In contrast, Spiers and Maguire (2006) had long-time residents navigate around the same virtual reality London used with TT, and found significantly increased activity in the hippocampus when subjects planned routes between start and destination points. In another fMRI study, the hippocampus was also significantly active when subjects, who had lived in London for on average 16 years, engaged in mental navigation (Kumaran and Maguire, 2005). Our findings in TT therefore suggest that the appearance of a navigation deficit in a remotely-learned and familiar environment following hippocampal damage may be dependent on the nature of that environment. The question that naturally arises is what aspect of a complex large-scale space is the hippocampus necessary for supporting? Our data also permit insight into this issue.

Whilst overall TT's navigation performance was significantly worse than control subjects, this was not an all-or-nothing result, a clear dichotomy across route trials was apparent. For some routes he was errorfree and others grossly impaired. The routes included in the test had been selected (based on pilot studies) to be likely, legal routes that sampled widely across central London, with minimum overlap between routes, and minimal effects of the video game. Thus, on the face of it, the reason for TT's pattern of performance was not obvious. We took our investigation further by conducting an in-depth analysis of the route characteristics. This allowed us to rule out a number of potential influences, such as physical features of routes (e.g. length, width, number of junctions and decision points, presence of major landmarks), factors related to TT (e.g. forgetting of destinations and making more errors at the start of a route), and to controls (e.g. TT's errorful routes were not more difficult for them than his errorfree ones, they made errors where TT didn't and vice versa). In fact, of 27 variables, only one was significant in relation to TT's pattern of performance. If a route contained a high number of non-A roads, then TT was impaired. Thus, he was able to navigate using main artery roads, but was unable to successfully negotiate the myriad of others that comprise the complex road matrix covering the city. What is it about non-A roads that makes them hippocampally dependent?

Perhaps it is related to how taxi drivers learn the layout of a city. Pailhous (1970) tested novice and expert taxi drivers in Paris and from this concluded that they learn to represent the city as a two-tier hierarchy. The base network consisted of the frequently used major arteries of Paris, with the secondary system defined as the other 90% of Parisian streets (Kuipers *et al.*, 2003). Licensed London taxi drivers, however, do not learn the layout of London by first learning the main artery roads, nor is this distinction made or highlighted as part of the testing. Thus, at an explicit level, this is not the framework around which the spatial representation of London is built. Perhaps non-A roads are used less frequently? As mentioned in the Results section, the taxi drivers had trouble dealing with the concept of frequency of use, as they had spent 40 years navigating in London, and everything was highly familiar, both A and non-A roads alike. Chase (1983) reports that in Pittsburgh, taxi drivers in fact try to spend more time off the main roads, and he found no evidence for the relevance of Pailhous' (1970) suggested two-tier spatial hierarchy. TT's performance on Route 3 may offer a further clue in this regard. There were no A roads on the Soho route yet TT performed normally. The Soho area of London has many small streets with a complex and dense layout, however some of the streets are very well known and we speculate that they might have acquired A road status. This would offer support for the idea that TT is able to navigate using main or frequently used roads. London taxi drivers have a saying, 'If in doubt, follow the yellow-brick road'. By this they mean if you're not sure about your route, stick to the main roads (coloured yellow/orange on the London map—*see* Fig. 4B). Thus, while impossible to get a measure of frequency of road use in long-experienced London taxi drivers, the A roads may have been experienced more and, over time, acquired a more semantic-like status, becoming independent of the hippocampus.

Although we ensured that the routes did not differ in terms of amount of salient landmarks, degree of visual detail and number of wide and narrow roads, the non-A roads are more densely packed together, and may be more visually similar to each other than the A roads. Gilbert *et al.* (1998, 2001) found that hippocampal lesions in rats impaired the ability to remember locations with increased spatial proximity, but memory for locations further apart was preserved. In a similar vein, Moscovitch *et al.* (2005, 2006) suggested that a schematic or coarse representation of topography can exist independently of the hippocampus. A loss of, or inability to access, fine-grained as opposed to coarse spatial representations could underpin TT's deficit.

One other issue in relation to TT (or any amnesic patient) should be considered when interpreting the findings. It could be argued that TT's residual hippocampal tissue might have been functionally viable, and facilitated the use of the A road network. It is known that residual hippocampal tissue can be active in the context of amnesia during fMRI scanning (Maguire *et al.*, 2001). However, given that TT's hippocampi were significantly damaged along their entire length, and that his amnesia was profound, we feel this explanation is unlikely. Alternatively, it might be argued that the representation of London in TT has nothing to do with the hippocampus at all, and the deficits we observed arise from damage elsewhere in the brain. TT had some general atrophy but retained intact perceptual, frontal-executive and language faculties. His spatial memory for London was also characterized predominantly by preserved function. Cumulatively this suggests a circumscribed spatial memory deficit compatible with focal damage. However, as in all cases of hippocampal amnesia, we cannot categorically rule out the possibility that there might have been hidden damage elsewhere.

Finally, our results have important theoretical implications. Three theoretical accounts of the time-scale of hippocampal involvement in remote spatial memory each make different predictions about a case like TT. If TT had been able to navigate normally, then this would have been support for the standard model of consolidation (Squire and Alvarez, 1995; Squire *et al.*, 2001). In this view, declarative memories (including spatial memories) over time become independent of the hippocampus, and rely instead on neocortical regions. However, TT was not able to navigate normally in this environment whose layout he learned almost 40 years ago. For the standard consolidation model to be true, the routes on which TT was impaired would have to have been learned more recently than the routes on which he was unimpaired. This was not the case; spatial memories for all routes were acquired in the remote past, and the A roads were not learned before the non-A roads during training.

By contrast, the cognitive map theory predicts that flexible navigation in environments learned recently or remotely would be impaired following hippocampal damage (O'Keefe and Nadel, 1978). That TT could not navigate normally around (virtual) London accords with this view. However, TT's exquisitely preserved performance on static tasks some of which involve allocentric information, is problematic for this view (Moscovitch *et al.*, 2006). In addition, it is not clear that a distinction between A and non-A roads can be made in terms of the allocentric information they embody or flexibility of the navigation they permit. Thus, while the cognitive map theory remains viable in its treatment of remote spatial memory, in its original form it cannot easily account for all of the findings from TT.

Based on the third theoretical model, the most recent formulation of the MTT (Moscovitch *et al.*, 2005, 2006), the prediction would be that TT could navigate in London to some degree, but with a deficit in the finer detail of his spatial representation. The data from TT seem most consistent with this view. His preserved coarse representation of the main artery roads may, over time and with frequency of use, have become semanticized, and so insulated from hippocampal damage. His impoverished representation or inability to access the fine details of London's layout may have prevented his rich re-experiencing of the city, thus compromising his navigation when it depended on non-A roads.

In conclusion, we believe the case presented here is unique in terms of the location of the lesions, combined with the history of taxi driving, and the novel means of testing and analyzing navigation performance. The findings show that the hippocampus in humans is necessary for facilitating navigation in places learned long ago, particularly where complex large-scale spaces are concerned and successful navigation requires access to detailed spatial representations. In the future it will be important to explore the precise conditions under which spatial representations remain dependent on the hippocampus, what level of detail is required, and exactly how this facilitates re-experiencing.

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