

Impaired Allocentric Spatial Memory Underlying Topographical Disorientation

Neil Burgess¹, Iris Trinkler¹, John King¹, Angus Kennedy² and Lisa Cipolotti³

¹*Institute of Cognitive Neuroscience and Department of Anatomy, University College London,*

²*Chelsea and Westminster Hospital and* ³*Department of Neuropsychology,
National Hospital for Neurology and Neurosurgery, London, UK*

SYNOPSIS

The cognitive processes supporting spatial navigation are considered in the context of a patient (CF) with possible very early Alzheimer's disease who presents with topographical disorientation. Her verbal memory and her recognition memory for unknown buildings, landmarks and outdoor scenes was intact, although she showed an impairment in face processing. By contrast, her navigational ability, quantitatively assessed within a small virtual reality (VR) town, was significantly impaired. Interestingly, she showed a selective impairment in a VR object-location memory test whenever her viewpoint was shifted between presentation and test, but not when tested from the same viewpoint. We suggest that a specific impairment in locating objects relative to the environment rather than relative to the perceived viewpoint (i.e. allocentric rather than egocentric spatial memory) underlies her topographical disorientation. We discuss the likely neural bases of this deficit in the light of related studies in humans and animals, focusing on the hippocampus and related areas. The specificity of our test indicates a new way of assessing topographical disorientation, with possible application to the assessment of progressive dementias such as Alzheimer's disease.

KEY WORDS

navigation, wayfinding, dementia, Alzheimer's disease

INTRODUCTION

Topographical memory allows a person to find or to learn to find his/her way from one location to the other, and is often impaired in dementia /56/. For example, patients with Alzheimer's disease have prominent deficits in topographical memory (referred to as 'topographical disorientation' [TD]) from an early stage of the disease /6,45/. However, topographical memory can also be selectively preserved in patients with semantic dementia /20, 50/. Thus sensitive tests for TD would be practically and theoretically useful, since it is one of the symptoms that could potentially differentiate between different types of dementia. Consistent with this, memory for sets of locations on a computer screen can be a useful predictor of the onset of dementia of Alzheimer's type /29,68/.

Although topographical disorientation, i.e. impaired navigation in daily life, may be relatively simple to diagnose in a patient's initial presentation, its formal assessment can be problematic. One problem is that TD is not a unitary cognitive function, but requires many different competences within which specific deficits could be quantified. As well as an ability to recognise landmarks, an ability to orient oneself with respect to them and knowledge of their relative locations are also required. In addition, places must sometimes be located relative to a set of distant landmarks rather than a single proximal landmark. A second problem is that only some of these competences (such as recognition of landmarks or spatial scenes) are

Reprint address:
Neil Burgess
Institute of Cognitive Neuroscience
University College London
17 Queen Square
London WC1N 3AR, UK
e-mail: N.Burgess@ucl.ac.uk

captured by current neuropsychological tests.

The majority of patients with TD show impaired recognition memory for landmarks and spatial scenes, which may well be the main cause of TD in these cases /30,34,38,46,53,62,67,70,81/. However, in a smaller number of cases, recognition memory is preserved /18,42,61,71/. These two patterns of impairment may reflect the need for both egocentric and allocentric information (i.e. knowledge of locations defined relative to the body or defined relative to the elements of the scene itself) in navigation, while recognition of a spatial scene from a fixed viewpoint can be achieved using either type of information alone. By contrast, recognition of a previously studied scene from a new viewpoint requires allocentric information, since objects or scene elements will still be located in the same positions relative to each other, but will no longer be in the same positions relative to the viewer /43/. We suggest that spatial memory from a shifted viewpoint provides a sensitive way of testing the allocentric component of navigation in large-scale space, and that this is not necessarily tested by current neuropsychological tests. For example, small-scale spatial tests in which the patient does not move relative to the to-be-remembered locations are highly susceptible to solution via an egocentric strategy.

Here we report a patient, thought to be in the very early stages of Alzheimer's disease (AD), who has topographical disorientation. She shows a striking dissociation between entirely spared static recognition memory for landmarks and severely impaired navigation. Interestingly, we document a dissociation between her memory for object locations when tested from a shifted viewpoint compared to when tested from the same viewpoint as at presentation. The selectivity of this impairment is accentuated by her preserved performance in all other aspects of mnemonic and spatial tasks (excluding only memory for faces). We suggest that this deficit in allocentric memory for the locations of places underlies our patient's poor navigation. In the discussion we speculate on the neural bases of this deficit, given the literature on related single-unit, lesion and neuroimaging studies in animals and humans. Notwithstanding this interesting speculation, and irrespective of the patient's eventual

outcome, this case indicates a new category of topographical disorientation: impaired allocentric spatial memory.

PATIENT REPORT

The patient was a 65 year-old right-handed writer who was referred for evaluation of progressive topographical memory and word finding difficulties. Neurological examination was normal, except for the cognitive deficits described below. A brain MRI scan contemporaneous with the experimental investigation was essentially normal. On the basis of the clinical history and the neuropsychological findings a clinical diagnosis of possible very early dementia of Alzheimer type was made.

Neuropsychological assessment

The results of the evaluation of the patient's cognitive deficits are shown in Table 1. On the Wechsler Adult Intelligence Scale-Revised /80/, her Verbal IQ was very superior and her Performance IQ was superior, broadly in keeping with her pre-morbid optimal level of functioning as estimated by the NART. Her performance on the Vocabulary subtest of the WAIS-R was also very superior. By contrast her performance on the Graded Naming Test /55/ was effortful and in the average range, suggesting the presence of mild word finding difficulties. Her literacy and calculation skills were normal. She scored in the very superior range on the NART reading test /59/ and the oral graded-difficulty spelling test /8/, and in the average range on the oral graded-difficulty calculation test /40/. Her performance on three tests sensitive to frontal lobe dysfunction was unimpaired (Wisconsin card sorting /58/; Stroop /73/; Trail Making B /4/). Similarly, her performance was within normal limits on a test of speed and attention (Part A of the Trail Making Test). Her performance of the perceptual and spatial skills subtests of the Visual Object and Space Perception Battery /79/ was entirely normal, including flawless performance on all the four subtests tapping space perception. Her performance of two tests of mental rotation was also unimpaired (the Flags test and the Little Man test /63/); see below for details of controls.

TABLE 1
Cognitive test scores

Verbal IQ	132	
Performance IQ	124	
NART IQ	126	
GNT Objects	20/30	(25-50%ile)
GDS	28/30	(>75%ile)
GDA	12/24	(50-75%ile)
Wisconsin card sorting test	6 categories	
Stroop	P	
Trail Making Test B	75 secs	(75-90%ile)
Trail Making Test A	35 secs	(50%ile)
Object Decision	19/20	(>5% cut-off)
Silhouettes	24/30	(50-75%ile)
Cube Analysis	10/10	(>5% cut-off)
Number Location	10/10	(>5% cut-off)
Position Discrimination	20/20	(>5% cut-off)
Dot Centre	10/10	(>5% cut-off)
Flags	10/10	(>5% cut-off)
Little Man	29/32	(control mean: 27, SD 6.3)

GNT = Graded Naming Test; GDS = Graded-Difficulty Spelling;
GDA = Graded-Difficulty Arithmetic; %ile = percentile; P = passed.

Memory investigation

The patient's husband reported that, despite having previously known part of London very well, in the year or so before the assessment she had got lost on occasion and had become very vague on how to get from one place to another. He also noted that she had become unable to understand the relationship among very familiar locations. Indeed, when she was questioned about her memory difficulties (by LC), she spontaneously reported that she had "difficulty in orienting herself even in familiar surroundings ... however, I had no problem in recognising the buildings". Her difficulties were exemplified by her impairment in describing two common routes within central London (e.g.

Houses of Parliament/Buckingham Palace; Bond Street/Oxford Street) and five very familiar routes in her neighbourhood. Indeed, for the two common routes within central London she stated that she would take a taxi since she was unable to recall the routes. Within her own neighbourhood, she was completely unable to describe the route to a local restaurant where she had dined regularly, at least once per month, over the last 10 years. Similarly, her description of the route to her local chemist was inaccurate. For three other very familiar locations, she was only able to give sketchy descriptions. These findings corroborate her and her husband's report of difficulties in navigating in previously well known areas including her own neighbourhood.

To explore her memory further the following

for unknown topographical material is far superior to her impaired recognition memory for unknown faces.

4. Semantic topographical memory

Three tasks assessed the patient's pre-morbid semantic knowledge of topographical information, using famous London landmarks, famous world landmarks and well-known maps. The famous London and world landmarks each consisted of a set of 15 coloured photographs. The maps were ten black and white outlines (see /19,54/ for details). The patient was presented with pictures, one at a time, and was required to name them. Her performance on these three tests was almost flawless (14/15, 15/15 and 10/10, respectively), showing well preserved semantic topographical memory.

EXPERIMENTAL INVESTIGATION

We used two new tasks to quantify her ability to navigate accurately in a new environment and to test the effect of changing viewpoint on her ability to remember locations. Both of these used adapted first-person perspective video games to present (on a computer screen) rich textured virtual environments within which the subject's viewpoint could be moved.

Control subjects

Four normal healthy women of comparable age (mean age 60 years, SD 3.1), education (to degree level), and IQ (estimated by Ravens Advanced matrices set I: mean 11 out of 12; standard deviation 1.3) to our patient were tested as controls on the Navigation and Spatial Memory tests described below, and on the Little Man test of mental rotation /63/.

5. Navigation in a virtual town

To directly assess the patient's ability to find her way around a new environment we used a virtual environment presented on a 15 inch computer screen (see /16,65,66/ for details). The patient and control subjects explored the town using a joystick for 15 minutes. The experimenter checked that they

had seen all parts of the town and that they felt that they knew where everything was. The patient and control subjects showed equal dexterity in following a marked path within the town as fast as possible (see Table 3). Subjects were then asked to find the shortest way from one location to a target location (a picture of which was constantly available as they travelled). If they failed to find a location after 4 minutes they were guided to it. The patient failed to find four of the ten locations, whereas all controls found all ten locations within the time allocated. In addition, the paths taken to the locations she was able to find were clearly abnormal. Firstly, they were obviously longer and less direct (the average path length was significantly longer than the control subjects'; see Table 3). Secondly, they involved several visits to incorrect locations, repeated failures to make the correct turn at a junction and a self-confessed lack of any sense of the direction to the target location. These results demonstrate a substantial impairment in navigation, and specifically in a newly learned environment, as well as her reported difficulties in previously familiar environments.

6. Shifted-viewpoint spatial memory

The patient's ability to recognise object locations from the same or from a shifted viewpoint was tested using a virtual reality town square that subjects look down into from the surrounding rooftops (see /43/ and Figure 1 for details). The square contains 21 randomly scattered plinths upon which objects can appear. Each trial consists of presentation and testing of memory for the locations of one, two or three objects. During presentation, the subject's viewpoint is fixed at one of two locations (about 135 degrees apart around the edge of the square) and one, two or three objects are presented sequentially for 3 seconds each. The screen is then blanked and, after a short pause, testing begins. In the 'same view' condition the subject sees the town square from the same viewpoint as at presentation. One of the objects then reappears at the same location as at presentation, accompanied by two foils (identical objects in different locations). The subject indicates which of the objects is in the same location as at presentation. This process is repeated for each of the (one,

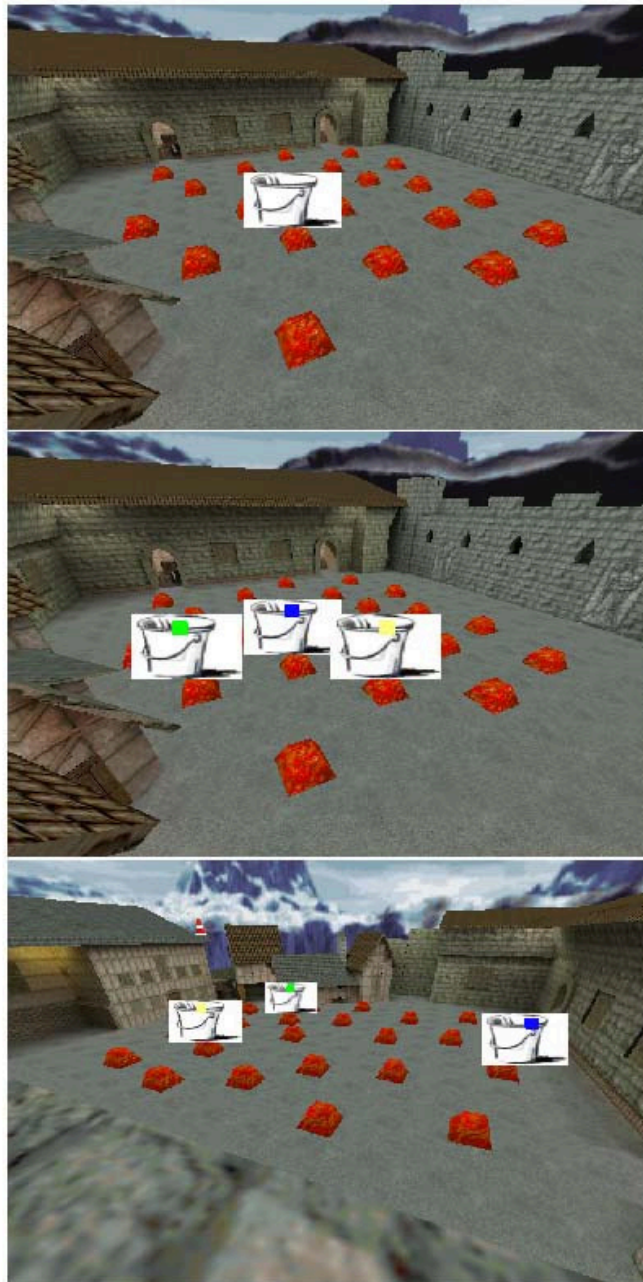


Fig. 1: The shifted-view object location task (shown in black and white – actual test is in full color). Top: example view at presentation. Middle: example view at test in the same-view condition: the subject should indicate that the object with the blue spot (shown as dark grey) is in the correct location. Bottom: example view at test in the shifted-view condition: the (tiny) traffic cone marks the viewpoint from which the subject experienced presentation, the subject should indicate that the object with the blue spot (shown as dark grey) is in the correct location. Note that the foil objects are closer to the target object in the same-view condition in an attempt to make it as difficult as the shifted-view condition.

TABLE 3
Experimental test scores

<u>Navigation test</u>			
	Patient	Controls	
		mean	(standard deviation)
Dexterity (speed) test	84 s	94 s	(34 s)
Average path length	200 m*	123 m	(25 m)
No. of failures	4/10*	0/10	(-)
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<u>Object-location test</u>			
	List length	Patient	Controls
			mean (standard deviation)
Same view	1	8/8	7.75/8 (0.50)
	2	15/16	14.50/16 (1.29)
	3	19/24	21.75/24 (2.06)
Shifted view	1	2/8*	6.00/8 (0.82)
	2	8/16*	12.00/16 (1.41)
	3	9/24	15.50/24 (3.87)
Difference (same – shifted)	1	6/8*	1.75/8 (1.25)
	2	7/16*	2.50/16 (1.29)
	3	10/24	6.25/24 (4.92)

* Significant difference between patient and controls (2 or more standard deviations).

two or three) objects presented. In the 'shifted-view' condition, the subject is tested in the same way, but is shown the town square from the viewpoint not used at presentation. In an attempt to match the difficulty of the two conditions, foils were presented on locations close to the target in the same-view condition (to make it harder) and far from it in the shifted-view condition (to make it easier). This strategy produces matched performance in healthy young subjects when three objects and five foils are used /44/, but failed to produce matched performance in this experiment, in which two foils were used to reduce the overall difficulty of the task (consistent with an age-related decrease

in ability in shifted-viewpoint tasks /37/).

The patient and controls were given eight trials at each list length (one, two and three) and tested on the same and shifted viewpoint conditions for a total of 96 responses from 48 trials of randomly interleaved types (see Table 3). Interestingly the patient's performance was similar to that of the controls in the same view condition at all three list lengths. In sharp contrast to this, her performance was noticeably worse than the controls in the shifted view condition, with the difference reaching statistical significance for list lengths one and two (increased variance due to one control subject prevented significance at length three); see Table 3.

Overall, the difference between the patient's performance in the two conditions was noticeably greater than that of the controls (significantly so for list lengths one and two, see 'same-shifted' in Table 3, and when pooled over all list lengths: $z = 2.53$). The pooled difference in performance between conditions was also considerably greater than the difference shown by the most similar individual control subject (23 versus 16). These results indicate a selective impairment in spatial memory from a shifted point of view.

DISCUSSION

Our patient, with possible very early AD, presented with grave topographical disorientation in the context of otherwise largely preserved cognitive skills. The neuropsychological assessment revealed well preserved intellectual, literacy, calculation, frontal executive, visuo-perceptual and visuo-spatial skills. Her ability to mentally rotate images was also intact. In addition, her verbal recognition and recall memory was preserved, including recognition memory for scenes, buildings and landscapes. She did, however, show a selectively impaired recognition of unfamiliar faces, and her ability to identify famous faces was poor, suggesting a general deficit in face processing.

Striking dissociations were found in the cognitive functions associated with topographical memory. Despite severe difficulties in describing very familiar routes and severely impaired navigation within a small virtual reality town, her memory for familiar and unfamiliar landmarks were remarkably intact. She was able to identify famous London and world landmarks as well as maps (and could recognise unfamiliar outdoor scenes, building and landmarks, as noted above). Interestingly, in the spatial memory test she showed an impaired memory only for the locations of objects in the town square when tested from a shifted viewpoint. Her memory for the locations of objects from the same point of view was essentially normal for the short list lengths tested (although there is a trend hinting that it might become impaired at longer list lengths). This finding, coupled with her intact spatial, perceptual and

mnemonic skills (excepting face recognition), suggests the presence of a selective deficit of allocentric spatial memory (or potentially of egocentric processes specific to the shifted-view task, such as those required to interpret the output of the allocentric system). We suggest that this specific impairment underlies the patient's navigational deficit in everyday life.

Previous tests specifically indicating a deficit in allocentric compared to egocentric spatial memory [35,43] did so in patients who showed a more general pattern of impaired recollection but spared recognition for a wide range of materials, such as words, faces, pictures [5,52,75]. In these cases, the allocentric deficit might be an important indicator of damage to the core processes required for memory retrieval when an exact match of the presented stimulus is not available, i.e. when familiarity-based recognition would be insufficient [2,44]. Conversely, however, the allocentric deficit might also be interpreted as secondary to the deficit in recollection. Here, for the first time, we describe a patient with a specific deficit of allocentric spatial memory but unimpaired free recall. This suggests that allocentric spatial memory is a specific category in its own right.

We suggest that our patient's spared egocentric memory allows her to perform in the same view condition of the spatial memory test, and also in the recognition of landmarks and scenes. Our patient's impaired allocentric memory may instead result in her navigational impairment. The ability to represent spatial locations relative to the surrounding environment (i.e. allocentrically) rather than relative to one's own body (i.e. egocentrically) is one of the requirements of navigation, since one will typically have moved along a long and complicated path since last seeing the target. An impairment to this ability may thus lie behind the patient's topographical disorientation, consistent with preserved performance in tasks testing many of the other functional requirements of navigation, such as recognising scenes and landmarks from the same point of view and mental rotation. We note that an inability to represent locations in an allocentric way is not necessarily a solely mnemonic impairment, and might also affect perception in a suitably-designed task.

Topographical disorientation has been described in terms of three core deficits /3/: 'egocentric disorientation' - impaired ability to represent the locations of objects relative to the self, associated with parietal damage; 'heading disorientation' - impaired ability to orient oneself relative to landmarks, associated with posterior cingulate (retrosplenial) damage; 'landmark agnosia' - impaired ability to recognise landmarks, associated with damage to the anterior lingual/posterior parahippocampal gyri. In addition a fourth category of 'anterograde disorientation' was tentatively suggested - impaired ability to create new environmental representations, associated with damage to the parahippocampal gyrus. A recent paper has associated this fourth category with processing in the hippocampus and consolidation to connected regions /74/.

The impairment we report here might be related to the 'anterograde disorientation' category, but would imply a specifically allocentric nature for the 'environmental representation', and would extend it to include the retrograde inability to recall familiar environments. Alternatively the deficit could be related to 'heading disorientation'. Even though the shifted-viewpoint test requires memory for object locations relative to landmarks rather than orientation of the self relative to the landmarks, it is possible that the task can be solved via mental manipulation of viewpoint within a stored egocentric representation. In this case being able to calculate one's orientation relative to the landmarks is a necessary intermediate step. However, in the clearest report of this (uncommon) category of impairment /71/, the two patients were able to describe object locations as long as they were all visible from a single viewpoint. Their impairment was described in terms of losing the sense of direction between one's own location and destinations within a space that cannot be entirely surveyed at one time. This is not consistent with our patient's deficit in the shifted-viewpoint task (in which the entire town square is visible from both points of view).

We can only speculate as to the neural basis of the patient's impairment, until such time as any progressive neurodegeneration becomes visible with structural imaging techniques. Several ana-

tomical loci are potentially plausible, based on previous work in humans and animals. We discuss some of these below.

The parietal lobes are traditionally associated with spatial processing. For example, parietal lesions in humans can lead to visuo-spatial neglect, optic ataxia and impaired mental rotation; single units in the intraparietal sulcus in monkeys encode the egocentric locations of salient stimuli in a variety of egocentric and allocentric reference frames (see /15/ for review). In addition, the parietal cortex has been implicated in path-integration in rodents: knowing where a goal location is based on one's own movements (see, e.g., /64/). However, our patient's preserved mental rotation and spatial-perceptual and spatio-motor performance argue against this locus.

The anterior lingual/posterior parahippocampal areas are most commonly associated with topographical disorientation. However, this is largely due to their implication in recognition of spatial scenes and landmarks /27,28,30,34,46,53,62,67,70/ arguing against this locus for our patient given her spared scene recognition, although we note that parahippocampal lesions can produce a delay-dependent deficit in an allocentric spatial memory task /11/. The patient's additional impaired processing of faces is also suggestive here. Processing of faces has been most closely associated with the fusiform gyrus /24,41,76/, and often co-occurs with impairments of scene recognition /46,53,62,69/. However, we note that recent studies have also implicated the perirhinal cortex (anterior parahippocampal gyrus) in face recognition /13,47/.

A small number of cases of 'heading disorientation' in the absence of landmark recognition deficits have been observed following retrosplenial damage /3,18,42,61,71/. Although the description of these patients' object-location memory is not entirely consistent with the profound shifted-view deficit in our patient, a retrosplenial locus would be broadly consistent with the suggestion that this area mediates translations between egocentric and allocentric representations /14,17,39/. In addition, the retrosplenial cortex is an important component of the circuit, including the hippocampus and head-direction system /72/, that supports navigation in rodents /2,25,31,48/. In this context it is thought to

support integration of visual and path integrative inputs in the representation of location /22/.

The area most clearly associated with good performance of the virtual reality navigation and shifted-view tasks is the hippocampus. A developmental patient (Jon /75/) with focal hippocampal damage /65/ was impaired on the navigation task (as were right temporal lobectomy patients /66/), and navigational accuracy correlates strongly with hippocampal activation in functional neuroimaging studies /33,36,49/. Most relevantly, Jon shows spared recognition of spatial scenes and objects, but was differentially impaired on the 'shifted-view' object-location task relative to the 'same-view' task /43/, even when both tasks were made equally difficult /44/. Jon's same-view performance was unimpaired for small numbers of objects (i.e. two or three) but became successively more impaired at longer list lengths, while his shifted-view performance was near chance for all list lengths above one object. This pattern may reflect a capacity limitation of egocentric memory, while allocentric memory is better able to form a combined representation of several object locations. Interestingly, our patient's same-view performance was beginning to fall below the controls' at list length three, and we avoided longer lists in case they were too taxing for our older controls. Implication of the hippocampus in allocentric versus egocentric spatial memory would be consistent with previous studies in humans /1,35/, rats /57/ and pigeons /9/, and with the recording of 'place cells' in rats /60/, monkeys /51/, and humans /26/ (see /7/).

Finally, we note the patient's impaired memory for even very familiar routes within her neighbourhood; this might also indicate damage to the basal ganglia. This area, and more specifically the caudate nucleus, appears to support an egocentric representation of routes that is built up over several repetitions of the route (see /32/ for a brief review of work in humans and rodents).

In summary, early involvement of the hippocampal formation or associated neocortical areas such as retrosplenial or perirhinal cortex may underlie our patient's impairment. Damage to the hippocampus or its entorhinal inputs would be consistent with AD /12/. In this case, the sensitivity of our spatial tests would be consistent with studies

showing a strong correlation between performance on a six-item object-location memory test and the transition of mild cognitive impairment to AD /68/. Although this task, which does not involve a shift of viewpoint, could be solved egocentrically, the list length of six probably favours allocentric processing. We predict that, unlike our shifted-view task, performance of this task at shorter list lengths (one, two or three) could be sustained by egocentric memory and so would not be such a good predictor of AD.

CONCLUSION

Current neuropsychological tests of memory for locations or spatial scenes can be solved on the basis of egocentric (viewpoint-dependent) memory alone. We suggest that allocentric memory for locations within an environment, i.e. knowledge of where the location is relative to other locations in the environment, forms an important component of topographical orientation and the ability to navigate accurately in large-scale spaces. Here we verified the navigational impairment of a patient with topographical disorientation using a virtual reality town /65,66/. We then probed the relative strengths of her egocentric and allocentric spatial memory by comparing memory for small numbers of object locations from the same point of view as presentation with memory from a shifted point of view /43,44/. We found a differential impairment of allocentric memory for object locations compared to egocentric memory. She also showed spared recognition of landmarks, object locations and spatial scenes from the same point of view, and unimpaired spatial abilities such as mental rotation. We suggest that her highly specific allocentric spatial memory deficit is the most likely single cause of her topographical disorientation. We speculate that this deficit may relate to as-yet imperceptible damage to the hippocampal system and related areas such as retrosplenial cortex. The shifted viewpoint test indicates a novel and sensitive way to quantitatively assess topographical disorientation in controlled circumstances and might potentially indicate a likelihood for progression to dementia of Alzheimer type.

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