

Using immersive virtual reality to test allocentric spatial memory impairment following unilateral temporal lobectomy

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ABSTRACT

Immersive virtual reality was used to investigate spatial memory in 17 right and 19 left unilateral temporal lobectomy patients and 18 control subjects. The subjects were administered a task consisting of a virtual room and table with radially arranged 'shells' on top. The subjects moved around the table and had to find a blue cube, which was under one of the shells. On subsequent searches, the cube moved to a new location and the subject had to find it whilst avoiding the previous location, and so on until all locations had been used. A selective deficit was observed in the right temporal lobectomy group only, linking allocentric memory to the function of the right hippocampal formation.

1. INTRODUCTION

Immersive virtual reality, in which the patient is physically able to move around in an imaginary environment, offers a promising new technique to explore spatial memory in a more realistic fashion, whilst maintaining experimental control. It also helps bridge the gap between non-human experimentation, where various forms of spatial mazes have been developed in order to help determine the neural basis for spatial memory. The immersive technique means that human analogues of the animal procedures can be developed for experimental use.

Both animal and human research point towards the hippocampal formation as being involved in spatial memory function. In animals, bilateral lesions of the hippocampus have been shown to result in deficits in spatial maze learning and single unit recording of cells in the hippocampi of rodents and monkeys demonstrate specific neurones that fire selectively according to the animal position or gaze direction in relation to spatial location (O'Keefe and Nadel, 1978; Rolls, 1996). These findings have led to the notion that the hippocampus may be involved in forming an allocentric representation of the environment, from which spatial memory is supported (O'Keefe and Nadel, 1978). This enables the animal to locate their position in space using external cues, irrespective of their bodily direction.

In humans large bilateral lesions of the hippocampus and surrounding temporal lobe regions produce global memory impairment. Unilateral lesions, however, result in modality specific or 'partial' amnesias depending on the side of lesion (Smith, 1989). This latter phenomenon has been established through investigating patients who have undergone unilateral neurosurgical treatment for intractable epilepsy. In order to remove a hippocampally based epileptic focus, a standard 'en bloc' operation involves taking out the anterior temporal lobe, the amygdala, the anterior two thirds of the hippocampus and surrounding cortical tissue. If this is done in a language dominant left hemisphere it produces verbal memory impairment; if in the right side, there is impairment in visuospatial memory function.

The pattern of visuospatial memory deficit has been explored through experimental studies. One of the main approaches has been to show the patient a series of objects layed out in front of them and then ask them subsequently to place the object from memory. Patients with right unilateral temporal lobectomies are impaired on this task (Smith and Milner, 1989). Furthermore, there is evidence that the extent of this deficit dissociates from remembering the objects. A recent study by Nunn et al (1999) showed that object recall could be matched between patients and controls by varying the delay between presentation and memory test

according to ability. Using these delays, there was still a pronounced spatial memory impairment in the right temporal lobectomy patients. The extent of this impairment was correlated with the amount of removal of the hippocampus.

The above type of task involves observing a static spatial array, with the possibility spatial location could be encoded in an egocentric sense, in relation to the bodily frame of reference. However, theories which link the hippocampus to spatial memory, incorporate the notion of an allocentric representation. A better test of previous theoretical approaches as applied to humans is to employ a task which is primarily allocentric in nature. A series of studies by Morris and his colleagues (summarised by Morris et al. 1999) have been conducted in this area. The first is a computerised task developed by Feigenbaum et al (1996). Here, a graphically represented turntable is presented on a computer screen. A number of spatial locations on the turntable were signified by black dots. The subject has to search these locations in turn, by touching each, with their response being recorded by a touch sensitive screen. When they touched the right one, the dot turned green. The correct location moved to another dot and the subject had to search again to find this new location, and so on until all the dots had been correct locations. In order to create an allocentric requirement, in between searches, the turntable would rotate such that the dots maintained the configuration in three dimensional, but not two dimensional space. Feigenbaum et al (1996) found that right unilateral temporal lobectomy patients were selectively impaired on this task.

The Feigenbaum et al (1996) relied on rotation of the spatial array, rather than subject movement, in order to induce an allocentric memory requirement. An alternative task was designed by Abrahams et al (1997) in which a real table was used, with a circular layout of containers. The experimenter would place some objects in some of the containers and then ask the subject to move round the table. They would then have to select the containers that had objects in them and also determine which objects had been placed in containers out of a larger sample. This task showed a selective impairment in right temporal lobectomy patients only, but with memory for the objects impaired in both left and right operated patients. Abrahams et al (1997, 1999) also tested patients who had selective unilateral damage to the hippocampus, finding impairment in only those with right lesions. Additionally, the spatial memory impairment was related to the amount of hippocampal damage as measured using structural magnetic resonance imaging. This contrasted with the finding that the amount of object memory impairment was related to the extent of reduction in temporal lobe volume, but not the hippocampus.

The Abrahams et al (1997; 1999) studies support the link between allocentric spatial memory and right hippocampal functioning. Furthermore, spatial memory tasks in general have consistently shown impairment associated with right temporal lobe damage. A criticism of these tasks is that they lack the experimental control needed to determine the specific mental processes involved in solving the task. For example, in the Abrahams et al (1997; 1999) study the patient could use extraneous room cues and associate these with specific locations, without recourse to spatial memory. To some extent this type of problem can be solved through darkening the room, but it is very difficult to rule out the use of visual cues in the environment completely. For this reason, Immersive Virtual Reality was adopted as means of providing complete control of the visual environment and at the same time developing a task which would involve whole bodily movement with corresponding visual mapping. A task was developed, termed the *Shell Task*, which consists of a virtual room which contains in the centre a virtual round 'table' (see Figure 1). Radially arranged on the table are up turned 'shells'. The object of the task is walk round the table in order to inspect each shell in turn. When a shell has been selected, a blue cube appears on the table in front of the subject. The subject then has to search the remaining shells in order to find one that triggers the appearance of the blue cube (in the task the subjects are told that the blue cube is under the shell). Each time the cube is found it moves to a new location, never returning to a previously used one. The task finishes when the cube has moved to all the locations. The task is to search for these different locations, whilst avoiding going back to a previous one. This task, to our knowledge, the first immersive virtual reality test of spatial memory, has been applied to patients with unilateral temporal lobectomies to further explore the link between allocentric spatial memory and the right hippocampal formation.

2. METHOD

2.1 Subjects

36 unilateral temporal lobectomy patients were included in the study (17 right; 19 left), seen a minimum of six month post-operatively. They were matched approximately for age and National Adult Reading Test estimated IQ with a control group of 18 subjects (respectively: Age Left: mean = 38.6, S.D. = 7.9; Right: mean = 36.4, S.D. = 10.2; Controls: mean = 38.8, S.D. = 5.9; IQ Right: mean = 111.9, S.D. = 9.6; Left: Mean = 104.4, S.D. = 8.3; Controls: Mean = 115.0, S.D. = 5.9). The patients has a standard en bloc resection, with between 5.5 and 6.5 cm of the anterior temporal lobe removed, the amygdala and approximately the anterior two thirds of the hippocampus.

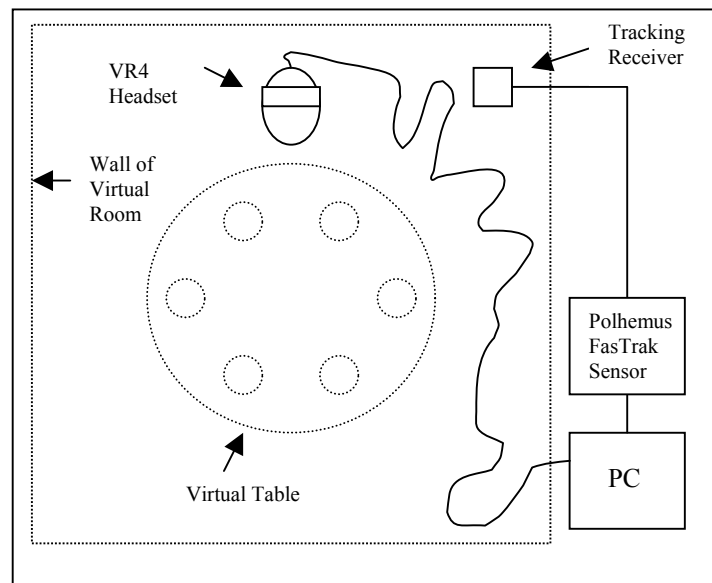


Figure 1. The layout of the Shell Task.

2.2 Virtual Reality Test

The World Tool Kit software package was used to construct the virtual environment, with the virtual room, table and shells (see Figure 1). A head mounted display (VR4 headset) projected the visual image to the subject and the position of the head was tracked using a Polhemus FasTrak Sensor system. This system tracks lateral, forward, backward and up and down movement of the head. The information is fed into the PC, with online processing of tracking data and image construction, which in turn changes the projected visual display.

2.3. Procedure

The procedure, termed the *Shell Task*, involves the subject standing in a room wearing the VR4 Headset. The subject stands in front of the Virtual Table (diameter 1.5m), facing the centre (see Figure 2). The Virtual Table is inside the Virtual Room (represented by dashed lines in Figure 1), which has 'bare' walls. The shells on the table are concave and coloured as indicated below, arranged radially. The subject has to walk around the Virtual Table and inspect the shells by 'looking under' them. In order to inspect a shell they walk in front of it and say the word 'lift.' This cues the experimenter to activate the removal of the shell using the PC keyboard. If the blue cube has been under the shell, it will then appear. If not, there is an empty space when the shell was placed. Following an inspection the shell returns to the original position.

The object is to search the shells until a blue cube is found. At this point it moves to a new location and the subject has to search again, and so on until all shells have had the blue cube under it. The subjects are instructed not to go back to shells where there has previously been a blue cube. Thus the design involves a series of searches to find the blue cube, a trial comprising the total set of searches.

In order to stop the subject using a simple search strategy of going round the table and inspecting each shell in turn, the following modification to the task was made. For each 'search' the subject is restricted to inspecting only half the shells. This is achieved by colour coding half of the shells green (those that can be

inspected) and the other half red (those that can not be inspected). When a search is finished (a blue cube is found), the shells that are green and red will change. Allocation to green or red is arranged pseudorandomly, with the exception that the target shell is always green.

After practice trials, the subject is tested in a version of the task with four shells for four trials. Next they have a six shell version, for three trials.

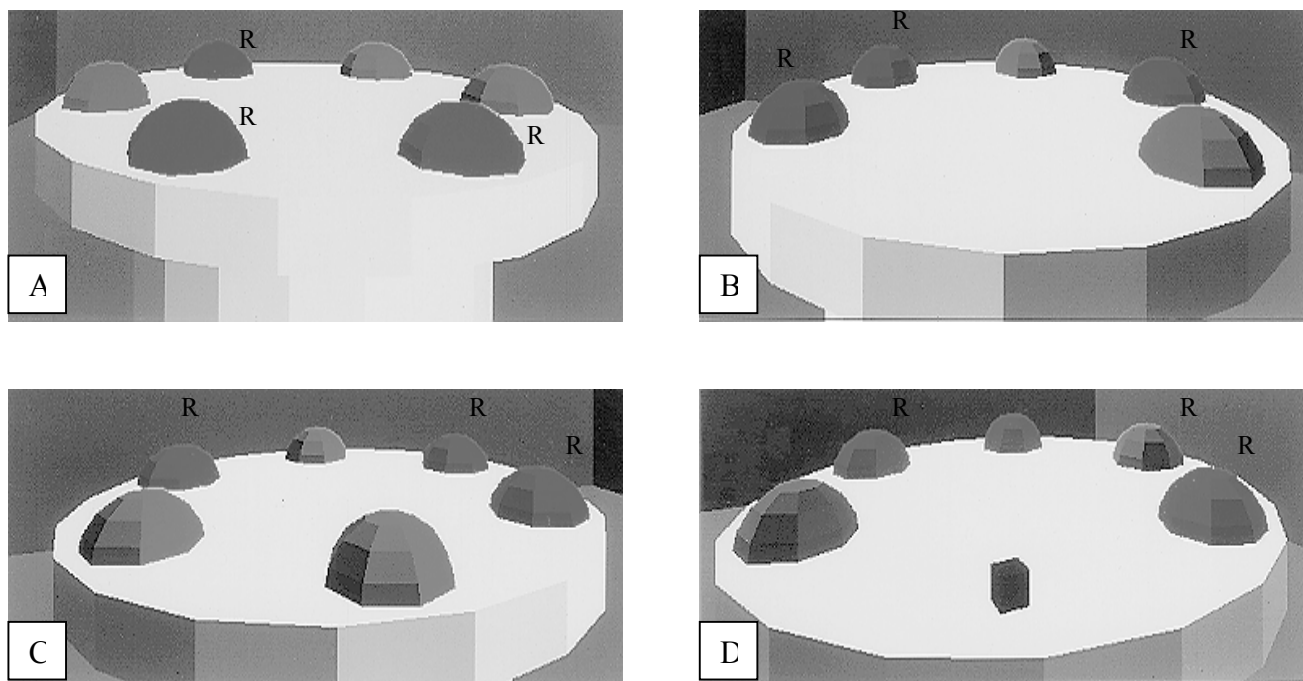


Figure 2. A series of views during a search for a blue cube. In this black and white illustration the restricted (coloured red) shells are labelled 'R.' (A) shows the layout at the start of the search; (B) shows the viewpoint when the subject has moved round the table and has just inspected a shell to reveal no blue cube; (C) the subject has move to the right and is just about to inspect a shell; (D) the shell is lifted and the blue cube is found.

3. RESULTS

The task generates two types of errors:

(1) *Within-Search* errors involve going back to a location that has been inspected previously within the same search. Here the errors were minimal (means for 6 shell trials: right TL = 0.00; left TL = 0.00; Controls = 0.02; means for 6 shell trials: right TL = 0.08; left TL = 0.08; Control = 0.07). No statistically differences were found between groups at either level.

(2) *Between-Search* errors involve selecting a shell that has had a cube underneath it on a previous search. The data are shown in Figure 3. For the fourth trial with four shells (4D) was included in order to check that the subjects could follow the procedures, whilst minimising the memory load. The shell was always to the right on the one under which the blue cube had been found. The very low error rate in this condition confirmed the subjects in each group were following the instructions correctly. This trial was excluded from the subsequent analysis. With six shells, there was a clear deficit in the right TL, contrasting with no deficit in the left TL group. The performance of the subjects can be compared to chance levels of responding, as shown in the control panel of Figure 3.

The data were analysed using a two-way MANOVA with group (right TL; Left TL and Controls) as a between-subject factor and shell number (4 and 8) as a within-subject factor (collapsing across Trial A-C). There was a main effect of Group ($F(1,51) = 5.19, P < 0.001$) and shell number ($F(2,51) = 3.61, P < 0.01$), with a significant interaction between the two factors. A subsequent analysis showed that the groups differed with six, but not four shells. For six shells, an ANOVA showed a main effect of Group ($F(2,51) = 2.68, P < 0.01$), and the Least Squares Differences (LSD) showed the right TL to be significantly impaired in relation to controls, but with no other significant difference. In addition, these analysis were repeated with age and

intelligence as covariate, but no difference in pattern was observed. Gender differences were explored using by repeating the main MANOVA with Gender (Male/Female) as an additional within-subject factor. No effect of Gender or interaction with the other factors was observed.

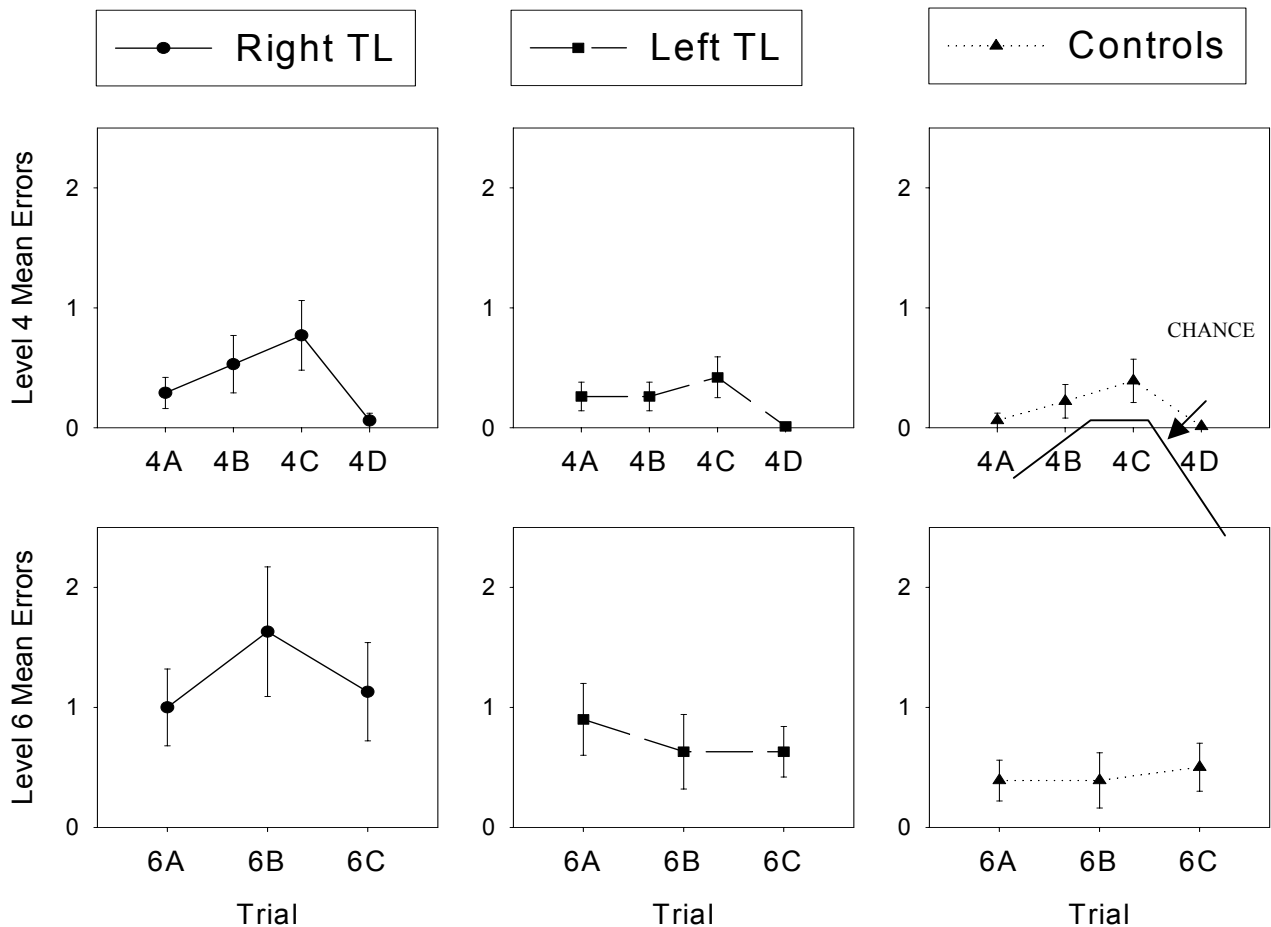


Figure 3. The between search errors on the Shell task, with standard error bars. The figure shows the performance of the right and left temporal lobectomy groups versus controls with the different trials for the four and six shell level (respectively 4A to 4D and 6A to 6C). The number of errors assuming chance level of responding are given in the panel for the controls (see text for the manner in which chance was calculated).

To illustrate movement performance, the trajectories of the subjects who completed the 6A trial using the same path up to the fifth search ($n = 33$) were classified by an independent who had no knowledge of what groups the subjects were in. On the basis of this, the subjects were divided into three categories: (A) those who were moving in a smooth and directed pattern; (B) those who showed some uncertainty in their movement and who would double back in their trajectory, and; (C) those with erratic movements. For category A there were 12 / 33 subject (7 controls; 7 left TL); For category B, 19 / 33 subjects (4 controls; 7 left TL and 11 right TL); For category C, 3 subjects (1 control; 1 right TL; 1 Left TL).

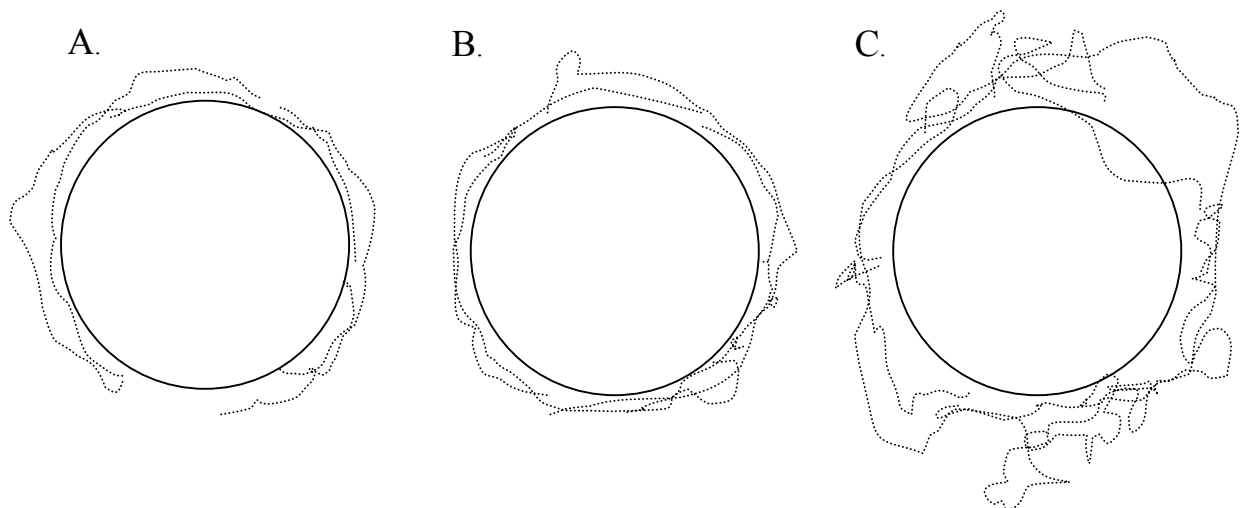


Figure 4. *Examples of the paths traced during a six shell problem. (A) is an example of a smooth and directed pattern. (B) shows doubling back or uncertainty in movements. (C) shows a highly erratic movement pattern.*

4. DISCUSSION

The study shows a clear spatial memory deficit in the right temporal lobectomy group, expressed in terms of the tendency to return to the previously successful shells. Very few errors were made in terms of returning to a previously successful location, suggesting that all groups were able to follow the task procedures. Additionally, errors were minimal on the fourth trial with four shells, this being designed to check for procedure before going on to the more difficult level.

In relation to the application of immersive virtual reality to testing spatial memory in this group of patients, this study shows that the technology can be used effectively. A number of practical aspects of task design are considered here before discussing the implications of the results in terms of understanding the neural basis of spatial memory. Firstly, the task was designed with a central table. This had the advantage of focusing the activity of the subject within a central space and the overall design enabled the task to stress the allocentric aspect of remembering location. However, we found that in order to complete the task, the subjects had to adopt the strategy of moving round the table whilst keeping their body facing the centre. Pilot studies had shown that, if they attempted to turn to the left or right and then rotate back towards the centre to view the table, this resulted in them being distracted from the memory aspects of the task. Consequently, we trained the subjects in terms of how to shuffle round the table in steady fashion, keeping the centre in view. We found that instructing the subject to make small movements ('small steps'), forwards or backwards, left or right, and then practising these movements enabled them to learn how to move correctly during the task. As indicated in the results section, a small proportion of subjects had difficulty with movement.

To truly exploit the advantages of immersive virtual reality, a much larger space would be needed, when the subject could walk around freely. This was not possible with the current technology, because the tracking mechanism had a limited range. Additionally, the ease of administration of the procedure was limited by the cable connecting the head mounted display to the computer. Technological innovations, combined with a larger workspace would substantially improve the scope for using immersive virtual reality to study spatial memory. A second aspect was the response mode used in the task. Originally, we had a glove mechanism such that the subject could 'touch' the shell in order to signal their inspection. Whilst this was a more elegant design aspect of the task, the effort the subject had to make in accurately touching the shells distracted them from attempting to remember the spatial locations. As a result, we adopted the simpler procedure of verbally instructing the experimenter whenever they wanted to select a shell. It is possible that immersive virtual reality could be eventually combined with speech reception to ease the interactive nature of clinical tests. More readily available in a reliable form, auditory feedback or instructional procedures could enhance this type of test, using stereophonic presentation. For example, when inspecting a shell, an associated noise could reinforce the interactive nature of the task.

The size of deficit shown by the right TL patients, although numerically small, is substantial when compared to the chance levels of performance. This level of deficit appears to be greater than that recorded with conventional 'desk top' tasks, for example in the studies by Nunn et al. (1998; 1999), where it is possible that the configurations within a small array was sufficient to ameliorate the size of the deficit. Further investigations are needed to explore how much the impairment translates into problems with everyday navigation ability. Questionnaire evidence does highlight problems with navigating in unfamiliar environments in patients with the right TL (Miotto, Feigenbaum and Morris, 2000). The current Shell task may be closer to the 'real world' than conventional psychometric tests that measure spatial memory function.

Checking the ability of the patients to follow the task procedure was an important feature of the overall design of the study. This was done by measuring the number of times the patients returned to the same shell within a search, but using trial 4D, the 'check trial,' and also considering the paths made by the patients. Overall, the study showed that the patients could 'cope' with the procedures as well as the controls. This was to some extent predicted in this sample patients. Temporal lobe damage is not associated with spatial manipulation or producing motor activity. Unilateral lesions in the regions of the temporal lobe resected do not produce perceptual deficits that could interfere with performance. Furthermore, overlapping samples of unilateral temporal lobectomy patients from related studies show no impairment on a range of tests of (non mnemonic) visuospatial processing. The right TL group are unimpaired across a range of mental rotation and spatial manipulation tasks (Abrahams et al., 1997; Feigenbaum et al., 2000; Worsley et al., 2000). However, using the same procedures to study memory in patients with more widespread lesions may be problematic, for example, parietal or frontal lobe lesions affecting respectively spatial processing and coordination of motoric output.

The current procedure had the advantage that the total visual environment of the subject was controlled, in a manner that had not been achieved so far when exploring this type of memory in patients with selective impairment. In previous studies it has not been possible to eliminate the strategic use of associating spatial locations with proximal stimuli, including those relating to the testing room or, possibly, imperfections in the testing apparatus. To exploit this aspect, the walls of the virtual room were left blank. This procedure forces the subject to adopt two types of approaches. One is to keep track of the configuration of the shells and monitor a starting location, based purely on visual information. A second it to monitor movement around the table to compute and encode location, perhaps using proprioceptive information. It is possible that both processes are used, and the current task does not enable us to disentangle these two possibilities. Certainly, there is evidence that monitoring of position relative to a fixed starting point (path integration) is impaired in patients with right TL, as shown in a recent study where patients were blindfolded and had to return to a starting point, after being led along two outward trajectories (Worsley et al., 2000).

A related issues is the neuronal distinction between visual processing, involving mainly pattern recognition, and encoding the spatial relations between objects. These types of processing are separated respectively in terms of perception, the visual analysis involving a neuronal pathway into the temporal lobe, and spatial processing the superior parietal region. Visual and spatial long-term memory has also been dissociated in patients with right temporal lobectomies (Nunn et al., 1998; 1999). The *Shell Task* has no distinctive object or environmental features, and hence relies more purely on spatial encoding. Thus the current study suggests that 'purely' spatial memory is impaired in the right TL patients, providing further support to the association between the hippocampal formation and spatial memory in humans.

6. CONCLUSIONS

In conclusion, an immersive visual reality system has been used to create a spatial memory test that has proved useful as an experimental tool to investigated memory impairment in patients with neurosurgical lesions effecting memory. The advantages of this approach from an experimental point of view have been discussed, and the clear finding of the experiment validates the use of this technology in this context.

7. REFERENCES

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