Allocentric spatial memory following anterior temporal lobectomy: A comparison between active and sedentary epileptic adults

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Compulsory declaration

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and in quotation in, this dissertation for the work, or works, of other people has been attributed, and has been cited and referenced.

Signature_____ Date_____

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ABSTRACT

The association between neural activity of the left hemisphere hippocampal region and verbal memory has been well established. Similarly, neuropsychological outcomes following left anterior temporal lobectomy (ATL) have been well documented, with deficits in the ability to learn new verbally encoded material consistently displayed. However, the association between non-verbal memory and functioning of the right hemisphere hippocampal region and, consequently, neuropsychological outcomes following right ATL, remains an area of debate. Moreover, relatively new evidence suggests that physical activity could improve overall hippocampal function (McCloskey, 2003). Therefore, the aim of the present study was to investigate spatial cognition in patients with intractable epilepsy and also to establish whether physical activity levels of these patients, i.e. active versus sedentary, had an effect on neuropsychological functioning. Spatial and verbal cognition were assessed in three groups: a pre-surgical (awaiting ATL) group, a post-surgical (following ATL) group and a healthy control group. Physical activity levels of all participants were established and left-sided damage and right-sided damage patient groups were divided into those with moderate-to-high activity levels and those with low activity levels. Results showed that on tests of spatial cognition, patients with right-sided damage tended to show more deficits than patients with left-sided damage when assessed using experimental tasks. However, no group differences were found when using standard clinical tests for assessment. On tests of verbal memory, patients with left-sided damage displayed more deficits than patients with right-sided damage. Patients with moderate-high activity levels performed better than patients with low activity levels on tests of spatial cognition, but both groups performed similarly on tests of verbal memory. The data therefore largely confirm the hypotheses. This is the first demonstration, within a single study, of spatial memory deficits using a virtual environment spatial navigation task in epileptic adults; and of an association between activity levels and improved spatial cognition on the CG Arena task in epileptic adults.

Introduction

Temporal lobe epilepsy (TLE)[1], of the intractable type, can be successfully treated by means of a surgical procedure known as an anterior temporal lobectomy (ATL). This procedure involves the removal of sections of temporal structures such as the hippocampus, parahippocampal gyrus, amygdala and uncus. These structures play a vital role in cognitive functioning, particularly verbal and visuospatial learning and memory. The removal of parts of these structures can therefore have a profound effect on cognitive functioning.

The association between verbal memory and the left hippocampus has long been established (Bell & Davies, 1998; Graydon, Nunn, Polkey & Morris, 2001; Seidenberg, Hermann, Dohan, Wyler, Perrine & Schoenfeld, 1996; Seidenberg, Hermann, Wyler, Davies, Dohan, Leveroni, 1998). Similarly, neuropsychological outcomes following left ATL have been well documented, with deficits in the ability to learn new verbally encoded material consistently displayed. However, the association between non-verbal memory and right hippocampus and, consequently, neuropsychological outcomes following right ATL, remains an area of debate.

In one example of typical research in this area, Kilpatric, Murrie, Cook, Andrewes, Desmond and Hopper (1997) investigated the degree of hippocampal atrophy and severity of memory deficits in 25 patients with temporal lobe epilepsy (18 with left-sided damage and 7 with right-sided damage), secondary to mesial temporal sclerosis. In each patient, MRI revealed unilateral hippocampal atrophy. Neuropsychological evaluations were carried out on the patients using subtests of the Weschler Adult Intelligence Scale-Revised (WAIS-R; Weschler, 1981), Rey Auditory-Verbal Learning Test (RAVLT; Rey, 1958), Rey-Osterrieth Complex Figure Test (RCFT; Osterrieth, 1944; Rey, 1941) and the Austin Maze (Cook, 1994). The Austin Maze is a measure of non-verbal topographical memory, requiring patients to discover a pathway, initially by trial and error. Patients are required to continue with the task until such time as they complete

[1] Temporal lobe epilepsy is a chronic neurological condition, characterized by abnormal electrical activity in the temporal lobe of the brain causing recurrent seizures (Penguin Dictionary of Psychology, 2001).

two trials of the maze without error. Results from their research identified a strong association between degree of left hippocampal atrophy and severity of verbal memory deficits. However, the same association was not identified between degree of right hippocampal atrophy and tests of non-verbal memory.

Lee, Yip and Jones-Gotman (2002) conducted a meta-analytic review of 33 studies that assessed verbal and non-verbal memory performance pre- and post-ATL. The results of their study showed a clear trend in verbal memory decline following left temporal lobe (LTL) resection; however, the pattern of memory change following resection from the right temporal lobe (RTL) was less clear. The authors concluded that further research was needed in order to confirm the relationship between the laterality of epileptic seizure, surgical resection from the temporal lobe and nonverbal memory.

One possible reason for the lack of clarity in the findings of Lee et al. (2002) could be that all of the studies included in that review made use of the Wechsler Memory Scale (WMS; Wechsler, 1974), specifically the Logical Memory and Visual Reproduction subtests. The authors suggested that their failure to find strong results could have been related to the insensitivity of the WMS Visual Reproduction subtest in detecting post-ATL non-verbal memory decline. Although the Logical Memory subtest showed reasonably good lateralizing value, the Visual Reproduction subtest did not, perhaps as the authors suggested, the test material can be easily verbalized.

Wilde, Strauss, Chelune, Loring, Martin, Hermann, Sherman and Hunter (2001) found similar results with regard to the WMS. The authors investigated the utility of the third revision of the Wechsler Memory Scale (WMS-III; Wechsler, 1997) in predicting laterality of impairment in patients with TLE. The authors found that WMS-III subtests were not able to distinguish between patients with left and right temporal dysfunction associated with unilateral seizure onset. They therefore suggested that the WMS-III not be used in isolation, but rather in the context of a comprehensive neuropsychological evaluation. Used this way, results from the test may prove more clinically useful.

The association between spatial memory and right hippocampus

One of the leading theories of hippocampal function was proposed by O'Keefe and Nadel (1978). Their "cognitive mapping theory" proposed that the right hippocampus was responsible for the processing of spatial information and that the left hippocampus was responsible for the processing of verbal information. Moreover, they proposed that the right hippocampus processes allocentric spatial information, rather than egocentric spatial information

Contrary to the cognitive mapping theory, Olton, Becker and Handelmann (1979) proposed the "working memory theory" suggesting that the function of the hippocampus is to process information relevant to the present situation or context. Working memory[2] is contrasted with reference memory[3], where information remains constant across situations. This theory has been supported by studies of hippocampal lesions in rats that displayed deficits in non-spatial working memory, but intact spatial reference memory processes (Koppelman et al., 1986; Olton & Feustle, 1981; Raphaele & Olton, 1988, as cited in Abrahams et al., 1996).

Abrahams, Pickering, Polkey and Morris (1997) then set out to examine spatial memory deficits in patients with unilateral damage to the right hippocampal formation. The authors used a task analogous to the radial arm maze and called it the nine-box maze test (NBMT). This task encourages the formation and utilization of allocentric spatial representations and provides measures of the four elements central to the two theories outlined above; object-working, object-reference, spatial-working and spatial-reference. Three groups of participants were involved in their study; a TLE group (including patients with right and left sided damage), and temporal lobe resection (TLR; including patients with right and left sided damage) group and a healthy control group. All three groups completed a neuropsychological evaluation, including the Rey Complex Figure Test, and the NBMT. Results showed that differences between the left and right groups were only present on the spatial memory measures. Both the TLE and TLR groups with right-

[2] Working memory consists of a memory system that holds the input while an interpretation of it is worked out (Penguin Dictionary of Psychology, 2001).
[3] Reference memory, also known as semantic memory, is simply memory for meanings (Penguin Dictionary of Psychology, 2001).

sided damage made more errors on the spatial components of the NBMT than the healthy controls, irrespective of the working versus reference memory distinction. Their study therefore provides support for the cognitive mapping theory of O'Keefe and Nadel (1978) rather than the working memory theory of Olton et al. (1979).

Egocentric versus Allocentric Spatial Memory

Spatial navigation in humans and animals is dependent on both allocentric and egocentric mapping systems. Feigenbaum and Morris (2004) described allocentric mapping as being "involved with identifying location relative to perceptible landmarks and encoding vectors between landmarks to provide a flexible system to determine location as the animal moves around the environment" (p. 462). They defined egocentric spatial memory as the "mapping system that identifies location in relation to the bodily axis . . . [it] is useful in navigation when the requirement is to remember locations from fixed positions" (p. 462). These authors conducted a study comparing egocentric and allocentric spatial memory following unilateral temporal lobectomy in humans. Participants were tested on a computerized human analogue of the Morris Water Maze (MWM; Morris, 1984), known as the Morris Maze Analogue (MMA). This task involved a graphically displayed swimming pool, presented on an upturned monitor. The participants were instructed to find a hidden platform by moving their finger around the pool; their movements were recorded by a touch-sensitive screen. This task was designed to provide measures of both allocentric and egocentric spatial memory.

Their study compared 30 participants who had undergone either right or left unilateral temporal lobectomy (14 RTL; 16 LTL), and 16 control participants. The neurosurgical participants had standard *en bloc* resections with the removal of tissue from the anterior pole, including the amygdala and anterior two-thirds of the hippocampus. All participants were tested a minimum of 6 months postoperatively. The authors concluded that allocentric, but not egocentric, spatial memory is impaired following unilateral temporal lobectomy in RTL participants. This finding supports the idea that the anterior temporal lobe, including the hippocampal formation, is involved in this function.

Further to this, Maguire, Burgess, Donnet, Frackowiak, Frith and O'Keefe (1998) conducted a study investigating the neural basis of navigation by humans, using functional neuroimaging of brain activity during navigation through a virtual reality town. Their study concluded that the right hippocampus and inferior parietal cortex cooperate to enable navigation to an unseen goal. The authors stated that the hippocampus provides an allocentric (environment-based) representation of space that allows the navigation from a particular start location to a goal location, and the right inferior parietal cortex uses this information to navigate toward the goal using correct body turns given the relative egocentric (body-centered) location of the goal and any obstacles that may be in the way.

Findings from Bohbot, Kalna, Stepankova, Spackova, Petrides and Nadel (1998) confirm the role of the right hippocampus in visuo-spatial memory tasks. Their study investigated verbal and spatial memory in patients who had undergone a surgical procedure (thermo-coagulation with a single electrode along the amygdalo-hippocampal axis) in order to alleviate their epilepsy. Patients with right-sided damage consistently displayed deficits on an object location task as well as on the Rey Complex Figure Test, whereas patients with left-sided damage consistently displayed deficits on the Rey Auditory-Verbal Learning Test.

More recently, Weniger and Irle (2006) investigated the role of the parahippocampal gyrus (PHG) in egocentric learning in a virtual environment. Three-dimensional magnetic resonance imaging (MRI) volumetric assessments were carried out on TLE participants in order to determine lesions of the hippocampus and PHG. All participants had undergone an ATL with removal of the temporal pole, the anterior perihinal, entorhinal and hippocampal cortices and part removal of the amygdala. Participants were tested, 3 years postoperatively, on a virtual reality task requiring the navigation in a virtual maze. Results showed an association between TLE subjects with right-sided posterior PHG lesions and impairment on virtual maze acquisition when compared to controls and TLE participants with anterior PHG lesions. The authors concluded that the right-sided posterior PHG plays a significant role in the representation and storage of egocentric information. Furthermore, the authors suggested that the combination of egocentric and allocentric information may facilitate the posterior PHG in constructing a comprehensive representation of spatial environments.

While the association between right hippocampus and spatial cognition has been established, there is some evidence suggesting that both the right and the left hippocampus play a role. Astur, Taylor, Mamelak, Philpott and Sutherland (2002) investigated spatial memory impairments, in a virtual Morris water task, in 10 humans with hippocampus damage. Five of the participants in their study had right-sided hippocampus damage and five had left-sided hippocampus damage. All 10 participants had undergone unilateral hippocampal removals as a component of temporal lobe surgery to treat medically intractable surgery. Participants were required to navigate through a 3-dimensional pool displayed on a computer screen using a joystick. The goal was to escape from the water as quickly as possible. The participant could escape the water by swimming over an invisible platform, which rose slightly once located. Each participant completed 20 trials with an additional probe trial during which the platform was removed from the pool. The participants then had to search for 30 seconds after which the trial automatically terminated. There was no indication to the participant that the probe trial was any different from the previous 20 trials until it was completed. These 20 trials plus the probe trial were then repeated. Results indicated that impairments in spatial learning/memory in a virtual Morris water task occur following unilateral hippocampal removal, but that these impairments occur regardless of the side of the seizure focus. While the authors acknowledged that this finding is atypical for learning/memory performance following surgery for epilepsy and that impairments on a task of this nature should be lateralized to the right hippocampus, this was not their finding. The authors therefore concluded that performance in this Morris water task is dependent upon bilateral involvement of the hippocampus.

Similar to the above findings, Incisa dellaRocchetta, Samson, Ehrle, Denos, Hasboun and Baulac (2004) found that side of damage did not affect impairment in spatial navigation. Their study investigated 21 patients with unilateral atrophy of the hippocampus secondary to long-standing epilepsy and 15 normal control participants. They were given three tasks measuring recall of egocentric or allocentric spatial location. The authors concluded that both right- and left-sided lesions resulted in significant impairment in memory for object location. These findings are contrary to previous studies (Bohbot et al., 1998; Feigenbaum & Morris, 2004; Jones-Gotman,

1986; Maguire et al, 1998) which have shown a clear association between right hippocampus and spatial memory deficits.

Evidence suggests that, while the association between left-hippocampus and verbal memory deficits has been well established, the association between right hippocampus and spatial memory deficits remains an area of debate. Therefore, spatial memory deficits in patients with right-sided damage as a result of temporal lobe epilepsy have proven difficult to detect. However, there is evidence to suggest that this association does exist. The present study aims to establish this association. Furthermore, considering the strong evidence for cognitive deficits, whether verbal or spatial in nature, the present study aims to investigate whether these deficits can be minimized, namely through exercise.

Epilepsy and exercise

There is considerable debate concerning the relationship between epilepsy and exercise, specifically that between exercise and seizure frequency (Arida, de Jesus Vieira, & Cavalheiro, 1998; Arida, Scorza, dos Santos, Peres, & Cavalheiro, 1999; Denio, Drake, & Pakalnis, 1989; Nakken, Bjorholt, Johannessen, Loyning, & Lind, 1990). Although some clinical and anecdotal observations suggest that exercise may induce seizures, empirical research has yet to provide verification for such an association. For instance, Arida et al. (1999), after conducting a study on rats, concluded that exercise did not lead to increased seizure occurrence within their experimental model.

In fact, most of the empirical evidence suggests that exercise actually *reduces* seizure frequency. For instance, Eriksen, Ellertsen, Gronningsaeter, Nakeen, Loyning and Ursin (1994) measured the seizure frequency of 15 women with pharmacologically intractable epilepsy who were participating in a 15-week exercise program. The participants exercised for 60 minutes twice a week and performed activities such as aerobic dancing with strength training and stretching. Participants recorded their seizure frequencies for 3-7 months before the intervention, during the intervention and for 3 months after the intervention. Results revealed that self-reported seizure frequency was considerably reduced during the intervention period. Additionally, the level of

subjective health complaints, such as muscle pains, sleep problems and fatigue, were also considerably reduced. However, most of the participants were unable to continue the exercise on their own after the intervention period and therefore, the exercise effects were not maintained during the follow-up period.

The effect of exercise on hippocampal function

It is an open question as to whether exercise has a positive or negative effect on human hippocampal functioning. In one such study to address this question Stroth, Hille, Spitzer and Reinhardt (2008) examined the benefits of aerobic endurance exercise on memory and affect in young adults. Specifically the authors investigated whether three running sessions of 30 minutes per week over a 6-week period had the potential to improve visuospatial and verbal memory, concentration performance and affect in healthy young adults. Twenty-eight students participated in the study and were divided into an experimental group, who took part in the training program, and a control group, who were asked not to vary their everyday activities. Results from their study showed a significant increase in visuospatial memory performance and positive affect; however, no effects of running training were observed on concentration performance or verbal memory.

Moreover, the effect of exercise on hippocampal function and specifically hippocampal related memory impairments as a result of seizure is an under-researched topic. In the only study, to the researchers' knowledge, to address this question, McCloskey (2003) proposed that physical activity could improve overall hippocampal function. His research was based on the general hypothesis (derived from, for example, the studies outlined in the previous section) that exercise will reduce the likelihood of seizure development, and will thereby reduce the hippocampal damage and consequent cognitive impairment associated with seizure. His experiment used two groups of rats (an active group, who had access to running wheels for 4 weeks, and a sedentary group, who did not have access to running wheels for four weeks, were injected with either an excitotoxic agent, kainic acid, or an injection of saline (a placebo). Kainic acid produces a prolonged seizure known as status epilepticus; this form of seizure is a common causative factor

in the development of human epilepsy and is also associated with memory impairments and reduced density of hippocampal neurons.

Results indicated that active animals were less likely to develop status epilepticus than those that were not active. Active animals also performed better on hippocampal-related memory, which was tested using the Barnes maze (Barnes, 1979). This task is used to evaluate spatial learning strategies in rats and other small rodents and is similar to the MWM. The author concluded that those animals with high exercise levels are less likely to develop seizures or to have hippocampal damage and related cognitive impairment following seizure.

Summary

There is much evidence suggesting the necessity for further research conducted on RTL and spatial memory (Bell & Davies, 1998; Lee et al., 2002). The literature suggests that failure to find significant results in the past could have been due to insensitive tests and/or examining the incorrect brain structures. The literature has also been unclear as to whether allocentric or egocentric spatial memory components, or both, are affected by right-sided hippocampal damage.

Furthermore, the present study aims to investigate whether the cognitive deficits associated with seizure can be reduced. Previous research (McCloskey, 2003) indicated that exercise may have a favourable effect on cognition. While many studies have been conducted in the area of exercise, hippocampal volume and spatial memory in rats and mice (Alaei et al., 2007; 2008; Ang et al., 2006; Asl et al., 2008; Clark et al., 2008; McCloskey, 2003; Trejo et al., 2008), few similar studies have been conducted on humans (Stroth et al., 2008; Eriksen et al., 2009).

Evidence therefore suggests that exercise improves hippocampal function and can also reduced cognitive impairment through limiting the likelihood of seizure development. The effect of exercise on hippocampal function in epileptic human adults, however, has not been explicitly established. This topic is therefore under-researched and further research, based on humans, rather than rats should be conducted, particularly in the context of epilepsy.

The proposed study, therefore, aims to assess allocentric spatial memory in 3 groups of participants: a pre-surgical group, a post-surgical group and a control group. The study will utilize tests sensitive to deficits in spatial memory. Further to this, active participants will be compared to sedentary participants in order to establish whether there are any significant differences and whether in fact exercise can reduce cognitive dysfunction associated with seizure activity. This study hypothesizes that the group of active adults will perform better on tests of spatial and verbal memory due to the preservation of the hippocampal formation at least partially as a result of exercise. Although similar studies have been conducted on rats, no such studies, to the researchers' knowledge, have been conducted on humans. For this reason, the importance of this study extends to the preservation of cognitive functioning of epileptic individuals through exercise.

Hypotheses

1. Right TLE/ATL patients will perform more poorly than left TLE/ATL patients on tests of spatial learning and memory. Conversely left TLE/ATL patients will perform better than right TLE/ATL patients on tests of spatial learning and memory and control participants will perform similarly to left TLE/ATL patients.

The rationale behind this hypothesis is that, as indicated by the literature, the right hippocampus is the area of the brain responsible for spatial memory. Therefore, it is expected that damage to right hippocampus will result in deficits in spatial memory.

2. Left TLE/ATL patients will perform more poorly than right TLE/ATL patients on tests of verbal learning and memory. Conversely, right TLE/ATL patients will perform better than right TLE/ATL patients on tests of verbal learning and memory and control participants will perform similarly to right TLE/ATL.

The rationale behind this hypothesis is that, as indicated by the literature, the left hippocampus is the area of the brain responsible for verbal memory. Therefore, it is expected that damage to left hippocampus will result in deficits in verbal memory.

3. Active patients will perform better on all neuropsychological measures than sedentary patients.

The rational behind this hypothesis is that if physical activity has a positive effect on brain functioning, it follows that patients with higher physical activity levels will perform better than those with lower physical activity levels.

Method

Design

This comparative, quasi-experimental study was quantitative and cross-sectional in nature. The logic of the comparative study allows approximation of causal inferences and a strong causal hypothesis (Mouton, 2001). A cross-sectional study involves data collection from a group of participants at a single point in time. This study compares specific cognitive abilities (spatial and verbal memory) in three groups of participants: a left anterior temporal lobectomy group, a right anterior temporal lobectomy group and a control group. In essence there are two independent variables, seizure focus and level of physical activity, which will be examined independently of one another. There are two major classes of dependent variables, which is based on sets of spatial cognition measures and verbal memory measures.

Participants

Two groups of adult patients were recruited from a private hospital in the Western Cape: a group of pre-surgical epileptic individuals (n = 13) and a group of post-surgical epileptic individuals (n = 16). A group of control participants (n = 30) was recruited from the University of Cape Town

and surrounding communities. Tests of allocentric and egocentric spatial memory, as well as tests of verbal memory, were administered to all three groups. Test scores were compared in order to examine the research hypotheses.

The selection of cases to form the samples adhered to the strict inclusion and exclusion criteria outlined below. The pre-surgical epileptic group was chosen according to the following inclusion criteria: pharmacologically intractable epilepsy, right/left hemisphere seizure focus, 18-50 years of age, and English proficiency. Participants were excluded from the group if one or more of the following were present: extratemporal epileptic focus, bilateral epileptic focus, malignant tumor, right hemisphere language representation, history of cerebrovascular accidents, previous brain surgery, dementia, hypothyroidism, history of head trauma with loss of consciousness, history of alcohol abuse and/or narcotic use, and history or presence of psychiatric disorders.

The post-surgical epileptic group was chosen according to the following inclusion criteria: anterior temporal lobectomy for treatment of pharmacologically intractable epilepsy 6-24 months prior to testing, right/left hemisphere seizure focus, 18-50 years of age, and English proficiency. The exclusion criteria were the same as those for the pre-surgical epileptic group.

The control group was chosen according to the following inclusion criteria: 18-50 years of age and English proficiency. The exclusion criteria were a previous history of epilepsy or any other factor mentioned above for the patient groups.

As can be seen in Table 1, participants in the three groups were matched, as closely as possible, with regard to age range, level of education and level of English proficiency.

Pre-surgical participants were recruited whilst awaiting surgery for the relief of intractable epilepsy. Each patient entering the hospital for such surgery was clinically and neuropsychologically evaluated by resident psychologists. Once the patient was admitted to the hospital they were connected to a monitoring system and weaned off their antiepileptic medications in order to induce seizures. These seizures were monitored in order to locate the seizure focus. Normally neuropsychological evaluations are completed within the first few days

of admission; it was only after this period that the experimenters for this study recruited suitable participants. On average there were one to two intakes per week and testing ran for approximately 6 months. However, approximately 50% of intakes during the 6-month period were excluded as they did not meet the requirements of this study.

The post-surgical group included patients who had previously had surgery at a private hospital in the Western Cape for intractable TLE. Contact details of these patients were obtained and each potential participant was contacted in order to establish their willingness and suitability to take part in the study. Those willing to participate were tested in their own homes.

Table 1
Demographic and Clinical Characteristics for Participants in the Current Study

	Preoperative Participants (n = 12)		Postoperative Participants (n = 16)		Controls (n = 30)
Variable	Right ATL (n = 7)	Left ATL (n = 5)	Right ATL (n = 6)	Left ATL (n = 10)	
Age	39.71 (6.45)	39.6 (11.72)	38.0 (8.79)	40.20 (8.35)	38.97 (7.93)
Gender (M:F)	2:5	1:4	3:3	2:8	12:18
Handedness (R:L)	7:0	4:1	6:0	8:2	26:4
Years of Education	13.57 (1.72)	14.60 (1.14)	14.00 (1.9)	13.50 (1.35)	13.91 (1.95)
English Proficiency score[a]	28.14 (1.77)	27.80 (1.79)	28.33 (1.51)	27.60 (1.51)	28.07 (1.55)
Age at Seizure Onset (years)	15.29 (11.66)	12.00 (7.45)	9.83 (3.43)	14.60 (8.76)	----
Duration of Disorder (months)	25.00 (9.75)	27.61 (15.3)	26.33(10.52)	25.59 (11.18)	----

Note. For all variables except Gender and Handedness, data presented are means with standard deviations in parentheses. ATL = anterior temporal lobectomy.
[a]Derived from the Human Science Research Council's Test of English Proficiency Test for South African adults.

Measures and Instruments

Screening Measures

A *sociodemographic and health questionnaire* (see Appendix A) was used to gather the following information: gender, age, years of education, handedness, population group, home language and medical history, such as age of seizure onset, seizure frequency and duration of disorder.

The *Human Sciences Research Council's Test of English Proficiency*, which was designed specifically for use in South African adult populations, examines whether or not the participant is proficient in English. The test consists of two sections, both featuring only multiple-choice questions. Section A requires the participant to read a paragraph and then fill in a missing word from a choice of four options. Section B requires the participant to choose, again from a set of four options, the correct word or phrase to complete a sentence. The maximum total score is 30. If a potential participant scored below 24 (the cut-off score for proficiency recommended by the test developers) he or she was excluded from further participation.

Measures of Spatial Memory and Learning

The Computer-Generated Arena

Measuring human spatial cognition by means of virtual environment (VE) tests has proved to be an accurate and reliable method (Feigenbaum & Morris, 2004; Weniger & Irle, 2006). The Computer-Generated Arena (CG Arena; Jacobs, Laurance, & Thomas, 1997) extends the MWM task to humans in order to test spatial memory. The CG Arena has proven to be a reliable and valid measure of different forms of spatial learning, memory, and navigation in humans across numerous studies (see, e.g., Jacobs et al., 1997; Jacobs, Thomas, Laurence & Nadel, 1998; Thomas, 2003).

The CG Arena utilizes a three-dimensional display on a computer screen as opposed to the actual maze used in the MWM. For the purposes of the current study, the CG Arena, consisting of

custom-designed software, was presented on a laptop computer. The participant viewed the screen from a first-person perspective and navigated around a multicoloured circular arena contained within one of three square rooms (a "waiting room", a "practice room" and an "experimental room"). In each of these rooms, the Arena was divided, for data analytic purposes, into four quadrants named Northeast (NE), Southeast (SE), Southwest (SW), and Northwest (NW). Boundary lines for the quadrants were not visible to participants. The experimental properties of the CG Arena used in this study are displayed in Table 2.

Each participant received standard verbal instructions on how to move through the CG Arena rooms. These instructions prepared the participant for the VE display, and directed him/her regarding how to navigate in the rooms as well as how to move from one room to another. Once the participant indicated that he/she was ready to start the task, the experimenter introduced him/her to the waiting room. This large square room featured four textureless walls, each of a different solid colour (blue, green, red and yellow), surrounding an arena that was defined by a circular wall with a marble texture. The ceiling of the room was light gray and the floor was dark gray. The purpose of the waiting room was, first, to allow the participant to practice navigating around the room and, second, to offer the participant the opportunity to rest between trials.

When the participant felt comfortable with navigating through the waiting room, or after a maximum of 60 seconds had elapsed, he/she pressed the space bar in order to continue with the experiment. This changed the display from the waiting room to the practice room. The practice room was identical in dimension to the waiting room; however, the walls were gray and there was a different picture on each wall. The participant had to locate a visible target (a large blue square) on the floor as quickly as possible within a time limit of 60 seconds. The visible target could easily be seen by the participant following a rudimentary scan of the environment. The task then was simply to move to the target as quickly as possible and stand on it. Once the participant located the target, a computer-generated clicking sound indicated success. The participant was allowed approximately 8 seconds to move around on the target before the trial ended and he/she was moved back into the waiting room. The target was in a different location on each of the trials, and the participant began each trial from a different starting point on the circumference of the arena. Participants performed a series of 4 visible-target practice trials to

make sure they had understood how to navigate in the CG Arena and what sort of task they would be faced with in the experimental trials.

Immediately after the 4 visible-target practice trials, the participant completed 8 hidden-target experimental trials. The experimental room was identical in dimension to the practice room; however, instead of one picture on each wall, there were three pictures on two walls and one picture on each of the other two walls, totaling eight pictures altogether. These trials also differed from the visible-target trials in that the target was hidden beneath the floor until the participant found it; the target was, however, always in the same place. The participant had 90 seconds in which to find the target. Once the participant moved onto the target it became visible and the computer-generated clicking sound could be heard. The participant was then allowed 8 seconds to move on the target before the trial ended and he/she was moved back into the waiting room. Participants could rest in the waiting room for up to a maximum of 120 seconds. As in the set of visible-target trials, the participant began each of the hidden-target trials from a different starting point around the circumference of the arena.

Immediately following the set of hidden-target trials, the participant completed a "probe" trial. Here, the previously hidden target was, unbeknownst to the participant, removed completely from the experimental room. This trial, which lasted 60 seconds was used in order to not only establish whether, and for how long, the participant would persist in searching for the target in its former location, but also whether the participant had been finding the target due to luck or whether they had actually established a robust cognitive map of the room. After completion of the probe trial the CG Arena program ended and participants were presented with a blank computer screen. Participants were then informed that the target had in fact been removed from the arena on the last trial; this debriefing served to prevent any possible anxiety associated with not being able to find the target.

Table 2.
Parameters for the CG Arena Used in the Current Study

CG Arena Phase	No. of Trials	Trial Time Limit	No. of Pictures
Practice Room	4	60 s	4
Experimental Room	8	90 s	8
Probe Trial	1	60 s	8

Note. Room dimensions were identical for all CG Arena trials: width = 100.00, depth = 100.00, height = 22.50. All measurements are in CG Arena Units, i.e., 10 units is equivalent to 1m, therefore 100.00 = 10m.

Following completion of the VE spatial navigation task, the participant was administered two pencil-and-paper companion tasks to the CG Arena: The Object Recognition Test (ORT) and the Arena Reconstitution Task (ART). These tasks provide measurements of spatial and non-spatial learning and memory that are independent of the arena and the data collected from it.

Object Recognition Test (ORT)

The ORT tested the capacity of the participants to recognize the pictures that were on the walls of the experimental room. The participant was presented with an A4-size laminated sheet on which 16 numbered pictures were presented in a four-by–four array (see Figure 1). Eight of the items were in the experimental room, and eight were distractors. The participant was asked to indicate, by circling either “yes” or “no” on an answer sheet, whether each item was in the experimental room.

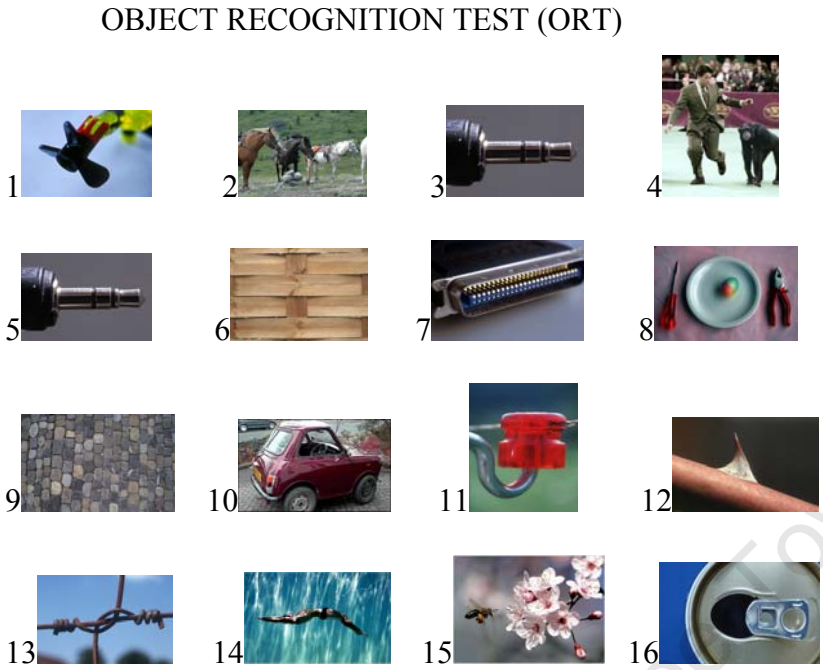

Figure 1. ORT Stimulus card

Arena Reconstitution Task (ART)

The ART, which was administered immediately following the ORT, required the participant to reconstruct the spatial layout of the room. The participant was given a stimulus card, similar to that shown in Figure 2, as well as eight small pieces of laminated cardboard, each bearing a representation of a picture from the experimental room. The participant was told that the stimulus sheet was a top-down representation of the experimental room, and was then asked to place each piece of cardboard in the appropriate space on the sheet. Finally, the participant was asked to indicate (by marking an "X" in one of the square boxes on the sheet) in which of the Arena quadrants the hidden target had been located.

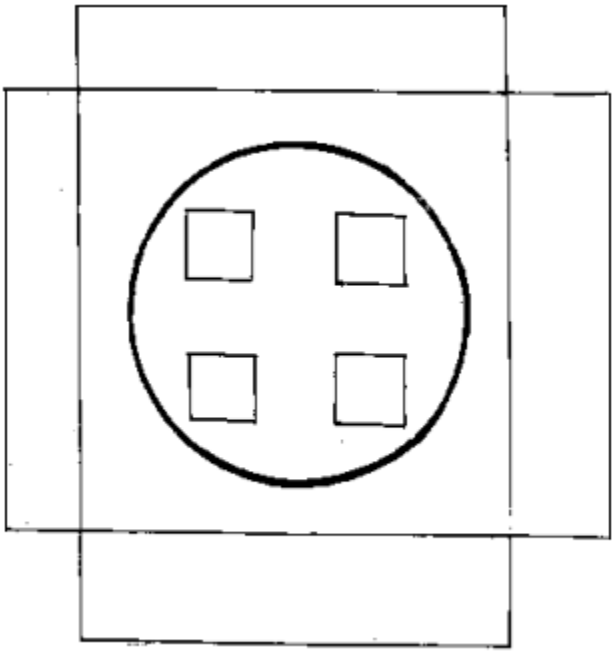

Figure 2. ART stimulus sheet

The Nine-Box Maze Test (NBMT)

The NBMT (Abrahams, 1997) was designed to compare spatial mapping and working memory theories of hippocampal function. As such, the task provides measures of spatial, object, working and reference memory. The spatial component of the test was specifically designed to encourage the formation of allocentric rather than egocentric spatial representations. This is facilitated by altering the participant's viewpoint of the spatial information between presentation and recall. Throughout all three stages of the task, participants were seated at a table with four chairs, one placed at each side of the table. The other items in the room as well as pictures on the walls remained constant throughout the task.

The NBMT consists of three stages: (1) object familiarization and free recall test, (2) the Five-Box Maze Test, and (3) the Nine-Box Maze Test (spatial and object memory test).

During the *object familiarization and free recall test*, participants were presented with 10 objects, viewing each for 15 seconds. After viewing an object, they were instructed to name and remember it and also to respond to the following question: "Would you carry this object

everyday in your pocket/handbag?" After presentation of all the objects and a 1-min filled delay, the participant had to recall as many objects as he/she could.

The Five-Box Maze Test (FBMT) serves as practice for the more demanding memory tests that follow. Materials for FBMT consisted of five identical containers and the first page of an object recognition picture booklet, which depicted five objects. On each trial two objects were placed in two containers and participants had to remember, independently, the two objects and the two containers (i.e., four pieces of information altogether). During a 1-min filled delay the participant was asked to change his/her position to one of the other chairs around the table and to continue with the simple interval filler task for the remainder of the delay. The participant was then shown photographs of five objects and instructed to point to the two objects that had been hidden.

The Nine-Box Maze Test materials consisted of nine identical cylindrical containers with detachable lids. These containers were fixed onto a square board in a circular formation, approximately 19cm from each other. The board was then positioned on an empty table with one chair situated at each of the four sides. The features in the room in which the table was placed remained constant throughout the test. Ten common everyday items were used as memory-testing stimuli; in this case, those items were a salt pot, a metal comb, two keys on a ring, a cigarette packet, an addressed envelope, a toy car, a clothes peg, a reel of cotton, four coins and a whistle on a chain.

This task consisted of five trials: one practice trial and four test trials. During each trial four objects were chosen and put into four containers. Participants had to remember the four objects that were hidden and which containers were used. They were not required to remember which items were hidden in which containers. After presentation of the four items and four containers, the participant had to change position to one of the other four sides of the board. In the following object memory test, the participant was shown an A4 page from the object recognition picture booklet containing all nine objects and was asked to pick out the objects that had been hidden. Each page in the object recognition picture booklet contained all nine items represented in a different array on each page. Participants were shown a different page on each trial. Following each response, the subject was given immediate feedback as to whether the choice was correct. If

the incorrect item had been chosen the participant was told that the choice was incorrect and was instructed to try again. The object memory test was complete after correct selection of four items or after a maximum of 10 choices. If the participant repeated a wrong choice, he/she was told that it was wrong but not that he/she had previously selected this item. If the participant repeated a correct choice, he/she was told that the choice was correct, but also told that that item had already been selected. During the location memory test the participant had to point to the containers that were holding the items. Completion of this task followed correct selection of 4 containers or after a maximum of 10 responses. The order in which the location and object recognition memory tests were administered was alternated between trials.

Objects were placed into the containers and the participant had to remember which containers contained an object as well as which objects were being used. The participant did not have to remember which objects were in which containers. Altering the participants' viewpoint of the to-be-remembered spatial information between presentation and recall facilitated the formation of allocentric spatial representations. This, effectively, discouraged the participant from being dependent on egocentric encoding; the latter strategy makes it particularly difficult to remember the spatial arrangement (Abrahams, 1997).

A fixed quasi-random sequence was followed regarding changing the participant's position around the table. The sequence included both clockwise and anti-clockwise rotations. Following each trial the participants maintained their new position for the next set of objects that were presented to be remembered; therefore, each participant experienced all four views of the board during presentation and memory stages.

Throughout the five trials, two of the selected objects and two of the containers remained constant, meaning that they were presented on each trial. These objects comprised the reference memory components of the task providing separate measures of object reference and spatial reference memory, respectively. The remaining objects and containers varied quasi-randomly between trials, in a fixed order. These items provided measures of object working and spatial working memory.

Rey-Osterrieth Complex Figure test (RCFT)

The RCFT (Osterrieth, 1944; Rey, 1941) is a test of visual learning and memory that requires participants to copy a complex drawing. After the initial copy, the participant is then required to draw the figure from memory (immediate recall) and to then draw it again after a 30-40-minute delay (delayed recall). This test is commonly used in research on epilepsy and cognition (see, e.g., Graydon et al., 2001; Hermann & Wyler, 1988; Kilpatrick et al., 1997; Kneebone et al., 2007; McConley et al., 2008). This test is also used extensively in clinical neuropsychological practice in South Africa.

Measures of Verbal Learning and Memory

Rey Auditory-Verbal Learning Test (RAVLT)

The RAVLT (Rey, 1958) was also used to assess verbal learning and memory. This task requires participants to recall as many words as possible from two lists of 15 words, each of which is read out loud by the examiner. The task consists of 5 learning trials for List A, during which a 15-word list is read to the participant, who then has to perform a free recall of as many words from that list as possible. After repeating this process five times, thereby giving the participant a chance to learn the list thoroughly, a new list (List B) is introduced. That list also contains 15 words, and the participant is asked to remember as many words from it as possible. After this distraction, a 6th trial requires participants to perform a short-delay free recall of List A. After approximately a 25-35 minute delay, a 7th trial requires participants to perform a long-delay free recall whereby they again had to remember as many words as possible from List A, without any further prompting.

The RAVLT has been used extensively in studies conducted on epilepsy and cognition (see, e.g., Äikiä et al., 2001; Kilpatrick et al., 1997; Loring et al., 2008; Pegna et al., 2002). This test is also used extensively in clinical neuropsychological practice in South Africa, and has been used in SA-based research studies (see, e.g., Thornton et al., 2008).

Wechsler Memory Scale-Third Edition (WMS-III) subtests

The Logical Memory and Paired Associate Learning subtests of the WMS-III (Wechsler, 1997) were used to assess verbal learning and memory. For the past several decades, the Wechsler Memory Scales have been a commonly used means of neuropsychological assessment in surgical centers for epilepsy (Raspall et al., 2005). Research on epilepsy makes extensive use of the WMS-III in neuropsychological evaluations (see, eg., Baker et al., 2003; Harvey et al., 2008; Seidenberg et al., 1998). This test battery is commonly used in clinical neuropsychological practice in South Africa; however, there is no published research featuring the WMS-III in South African populations.

The immediate recall portion of the Logical Memory subtest (LM I) consists of the examiner reading two short stories to the participant; each reading is followed by a request for the participant to retell the stories from memory. The second story is presented twice. After 25-35 minutes, the participant is required to attempt delayed free recall of each story in turn (LM II).

The immediate recall portion of the Paired Associates Learning subtest (PAL I) consists of four trials, each with eight word pairs. Each trial proceeds as follows: The examiner reads out each word pair at a rate of one per second, giving the participant approximately 2 seconds between pairs. After the reading, the examiner starts again from the top of the list, giving the participant the first word from the pair and asking him/her to remember the second word from the pair. The same eight word pairs are used over all four trials, but are presented in a different order on each trial. After 25-35 minutes, the participant is required to attempt delayed free recall of the word pairs (PAL II).

Measures of Physical Activity

World Health Organization's (WHO) Global Physical Activity Questionnaire (GPAQ) version 2.0

The GPAQ (see Appendix D) was developed by the WHO (2002) for physical activity surveillance. This questionnaire collects information on participation in physical activity in three

different settings (at work; travel to and from places; and recreational activities), and also evaluates sedentary behaviour. Participants answered questions according to how many minutes or hours they participated in certain activities.

Procedure

Once a potential participant had been identified, that individual was given an informed consent sheet (see Appendix B) detailing the nature and purpose of the study. These details were discussed with each participant, ensuring their understanding of the requirements of their participation in the study as well as contact details for the chief investigators. Once the participant had read, understood and signed the informed consent document, the experimenter continued with the sociodemographic and health questionnaire. Once this questionnaire was completed, the experimenter continued with the remainder of the tests.

Pre-surgical participants were tested at their hospital bedside and completed the HSRC Test of English Proficiency, GPAQ, CG Arena, ORT, and ART. Verbal memory scores were obtained from the resident psychologists' neuropsychological evaluation. The NBMT was not administered to the pre-surgical group of participants due to logistical reasons (primarily, the inability to remove them from their hospital beds). Once they had been placed on monitoring their specialists were reluctant to have them taken off, as this removal could have resulted in seizures not being recorded, thus compromising the process of locating seizure focus.

Post-surgical and control participants completed the informed consent documents in identical fashion to that described above, and the completed all of the test materials, as listed above. Table 3 presents a timeline of study events.

Table 3.
Timeline of Study Events

Time (mins) from Study Start	Event
00.00	Informed consent; sociodemographic and health questionnaire
05.00	HSRC Test of English Proficiency
15.00	GPAQ
20.00	RAVLT: immediate recall
35.00	WMS-III: LM I and PAL I (immediate recall)
55.00	RCFT: copy and immediate recall
65.00	RAVLT: delayed recall
70.00	CG Arena, ORT, and ART
100.00	WMS-III: LM II and PAL II (delayed recall)
120.00	RCFT: delayed recall
130.00	NBMT (omitted from pre-surgical events)
150.00	Debriefing

All of the standard clinical tests (HSRC Test of English Proficiency, GPAQ, WMS-III subtests, RCFT, and RAVLT) were administered following the conventions outlined in either administration manuals or textbooks (Lezak, 2004). The experimental tasks (NBMT and CG Arena) were administered following the conventions outlined in previous research studies employing these instruments (e.g., Jacobs et al., 1997; 1998).

Each assessment session lasted approximately 120-150 minutes, and concluded with a short debriefing. During this debriefing, the participant had the opportunity to ask questions which were then answered, as fully as possibly, by the experimenter. All participants were reassured that they performed well in all the tests, but were told that, following standard research protocol, individual test results would not be given to them. They were also reassured that their individual scores would never be presented in the write-up of the study, and that those scores would not be available to anyone other than the investigators.

Data Analyses

Test Scoring

The HSRC Test of English Proficiency yielded a total score out of 30. All correct answers were added together in order to obtain this score.

The GPAQ was scored as follows: Each question was coded (P1, P2, P3, etc). The following equation was used in order to establish a score for each participant: Total physical activity (TPA) = [(P2*P3*8) + (P5*P6*4) + (P8*P9*4) + (P11*P12*8) + (P14*P15*4)]. In order to establish whether activity levels are high, moderate or low, the following calculations were done: A participant was classified as highly active if P2 + P11 > 3 days and TPA minutes per week were more than 1500, and moderately active if P2 + P11 > 3 days and [(P2*P3) + (P11*P12)] > 60. Low activity levels were values that did not reach the criteria for either high or moderate levels of physical activity.

The RAVLT produced measures of encoding, acquisition, short-term percent retention (STPR), long-term percent retention (LTPR), and learning over trials (LOT). The total number of words recalled on Trial 1 gave a measure of encoding. The total number of words recalled over Trials 1-5 gave a measure of acquisition. The following equation was used to calculate STPR: (number of words recalled Trial6 / number of words recalled on Trial5) x 100. The following equation was used to calculate LTPR: (number of words recalled on Trial7 / number of words recalled on Trial 5) x 100. The following equation was used to calculate LOT: Acquisition – (5 x Trial 1).

In order to score the WMS-III Logical Memory I (immediate recall) subtest, the two stories were broken down into units (e.g., "Anna" was one unit, "Thompson" was one unit, "of South" and "London" were another two units). If the unit was present in the participant's recall of the story, the participant was awarded 1 point; if it was not present, the participant was given 0 points. For each story, the maximum score was 25. The total of these two scores together (the recall of the first story plus the first recall of the second story), yielded a 1st Recall Total Score, which ranged from 0-50. Logical Memory II (delayed recall) was scored in identical fashion.

The WMS-III PAL subtest also yielded two scores, an immediate recall score and a delayed recall score. The immediate recall total score ranged from 0-32, and was calculated using the sum of the correct answers given across the initial four presentations of the word pairs (PAL I); 1 point was given for each word pair correctly recalled. The delayed recall total score ranged from

0-8, and was calculated using the sum of the correct answers given during PAL II; again, 1 point was given for each word pair correctly recalled.

The RCFT was scored according to the Taylor scoring system (Lezak, 2004, p. 812). Briefly, the figure was broken up into eighteen units and 0-2 points were awarded for the correct placement and correct drawing of each of the eighteen units, giving a maximum score of 36 for each of the copy, immediate recall, and delayed recall portions of the test. The copy score was not used in the final analyses because all participants should perform similarly on the copy. No spatial memory is required to simply copy a complex figure. Any deficits present at this level would be perceptual in nature rather than purely spatial.

CG Arena software generates a unique data file for each participant on each trial. This data file includes information about how long (in seconds) the participant took to locate the target, how long the path was from start point to target, and how much time the participant spent in each quadrant of the arena on each trial. (For more information on what is contained in these data files, see Jacobs et al., 1997, 1998, and Thomas et al., 2001.) These outcome variables, named "Total Time" and "Length to Target" were used in the analysis of CG Arena performance.

To score the ORT, a d-prime (*d'*) score was derived for each participant. D-prime is a commonly used measure of sensitivity in signal detection theories, representing the difference between the means of the "signal present" and "signal absent" distributions. To calculate *d'*, the participant's hit (H) and false alarm (FA) rates were used in this formula: $d' = z(\text{FA}) - z(\text{H})$. Specifically, FA and H are the false alarm and hit rates that correspond to right-tail probabilities on the normal distribution, and therefore $z(\text{FA})$ and $z(\text{H})$ are the standard scores that correspond to the right-tail *p*-values represented by FA and H. Larger absolute values of *d'* mean that a person is more sensitive to the difference between the "signal present" and "signal absent" distribution. Values of *d'* that are near zero indicate chance performance. (See http://wise.cgu.edu/sdtmod/signal_applet.asp for more details).

To score the ART, each icon that the participant had placed on the stimulus sheet had a number underneath it. The place in which each icon had been set was recorded by writing the appropriate

number in the appropriate place on the stimulus sheet. The ART was then scored following the rubric outlined in Appendix C. Participants were given 1 point for each correct item on the score sheet, yielding a total maximum score of 10.

The major performance measure derived from the NBMT was the total number of errors made by each participant before making the correct selection. If items were not correctly selected, the maximum score was 10 errors. Therefore, the higher a participant scored, the worse their performance; conversely, the lower a participant's score, the better the performance on the task. The scores were totaled separately across four trials for each of the four memory components. This scoring system produced four memory measures (spatial-reference, spatial-working, object-reference and object-working) for each participant.

Descriptive Statistics

Mean scores and standard deviations are presented under the results section below, for each dependent variable.

Inferential Statistics

All statistical analyses were performed using the software packages Statistica version 7 (StatSoft, 2004) and SPSS version 15.0 (SPSS Inc., Chicago IL). The statistical significance threshold was set at $\alpha = 0.05$. Details of each individual analysis are presented under the Results section below.

Results

Spatial Cognition

CG Arena: Visible target trials

Descriptive statistics for the path length taken by participants from start point to target location on these trials are presented in Table 4. The set of visible target trials were, as noted earlier, designed to ensure that all participants, regardless of prior computer gaming experience, were well trained in the presentation and requirements of the CG Arena before moving onto the next, crucial, phase of the spatial navigation task. If, as is the case with most mixed male-female samples, there is great variation in prior computer gaming experience, then one should expect to see more variability in performance on the first few visible target trials, but a rapidly decreasing amount of variability toward the end of that set of trials. Table 4 shows that this is in fact the case: Generally speaking, there is less variability in performance on later trials than on earlier trials, an indication that participants (regardless of group) are becoming more proficient at moving within the VE and at locating the target.

Table 4.
Descriptive Statistics for CG Arena Path Length: Visible target trials

	Trial 1	Trial 2	Trial 3	Trial 4
Pre-ATL-R (*n* = 7)	76.54 (30.18)	54.61 (25.60)	36.51 (13.41)	57.65 (12.09)
Pre-ATL-L (*n* = 5)	68.33 (20.30)	50.14 (32.39)	34.05 (12.57)	64.03 (19.92)
Post-ATL-R (*n* = 6)	95.33 (83.55)	91.66 (45.51)	64.50 (44.94)	85.33 (30.66)
Post-ATL-L (*n* = 10)	76.53 (28.55)	66.85 (43.45)	45.92 (26.66)	62.52 (19.29)
ATL-R (*n* = 13)	85.21 (58.80)	71.71 (39.50)	49.43 (33.79)	70.43 (25.90)
ATL-L (*n* = 15)	93.80 (25.73)	61.28 (39.75)	41.96 (23.15)	63.02 (18.90)
Control (*n* = 30)	81.69 (30.13)	66.45 (42.20)	45.09 (30.62)	57.56 (9.31)

Note. Mean scores are presented, with standard deviations in parentheses. Pre-ATL-R = pre-surgical anterior temporal lobectomy, right-sided seizure focus. Pre-ATL-L = pre-surgical anterior temporal lobectomy, left-sided seizure focus. Post-ATL-R = post-surgical anterior temporal lobectomy, right-sided surgery. Post-ATL-L = post-surgical anterior temporal lobectomy, left-sided surgery. ATL-R = pre- and post-surgical anterior temporal lobectomy groups combined; ATL-L = pre- and post-surgical anterior temporal lobectomy groups combined. These acronyms are consistently used in many of the tables that follow.

The prediction for this outcome variable, therefore, was that there would be little or no observable difference between the groups over the set of 4 trials. Otherwise stated, all participants, regardless of group, should be performing at more or less the same competence level by the end of the four visible target trials. Statistical analyses, using repeated-measures ANOVA, confirmed this prediction.

The first set of comparisons was conducted between the pre-ATL-R, pre-ATL-L and control groups. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of trials, $\chi^2(5) = 21.239$, $p = .001$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .723$). There was a statistically significant main effect of trials on path length to find the target when testing within-subjects effects, $F(2.169, 84.605) = 9.101$, $p < .001$. However, the trials x group interaction was statistically non-significant, $F(4.339, 84.605) = .445$, $p = .791$, as was the main effect of group, $F(2, 39) = .647$, $p = .529$.

The second set of comparisons was conducted between the post-ATL-R, post-ATL-L and control groups. Mauchly's test this time indicated that the assumption of sphericity had been upheld, $\chi^2(5) = 10.329$, $p = .067$. There was a significant main effect of trials on path length to find the target when testing within-subjects effects, $F(3, 129) = 5.332$, $p = .002$. However, the trials x groups interaction and the main effect of groups were again statistically non-significant, $F(6, 129) = .132$, $p = .992$, and $F(2, 43) = 3.200$, $p = .051$, respectively.

The third set of comparisons was conducted between the ATL-R (a group combining all pre-operative participants with right-sided seizure focus with all post-operative participants who had undergone right anterior temporal lobectomy), ATL-L (a group combining all pre-operative participants with left-sided seizure focus with all post-operative participants who had undergone left anterior temporal lobectomy) and controls. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of trials, $\chi^2(5) = 12.75$, $p = .026$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .884$). There was a significant main effect of trials on path length to find the target when testing within-subjects effects, $F(2.653, 145.900) = 11.429$, $p < .001$. However, the trials x group interaction

and the main effect of group were again both statistically non-significant, $F(5.305, 145.900) = .218$, $p = .960$, and $F(2, 55) = .820$, $p = .445$, respectively.

In summary, these three analyses show that for the pre-ATL comparisons, the post-ATL comparisons, and the combined-group comparisons, all participants, regardless of group, improved over trials such that there were no statistically significant between-group differences. Therefore, by the time participants got to the final visible target trial, they were all at approximately the same level of competence with regard to the visuoperceptual and motoric demands of the VE task. The visible target trials therefore served their purpose of familiarizing participants with the VE and making sure that they understood what was expected of them before moving on to the invisible target trials.

CG Arena: Invisible target trials

Descriptive statistics for the path length taken by participants from start point to target location on these trials are presented in Tables 5 and 6. It should be noted here that one participant had a seizure during testing and was unable to complete Trial 6. The average score for this group on Trial 6 was used to replace the missing score.

The predictions for this outcome variable were that participants in the pre-ATL-R group would perform worse than those in the pre-ATL-L group; that participants in the post-ATL-R group would perform worse than those in the post-ATL-L group; and that participants in the ATL-R group would perform worse than those in the ATL-L group. Furthermore, it was predicted that participants in the control group would perform significantly better than those in the pre-ATL-R, post-ATL-R, and ATL-R groups, but would perform similarly to participants in the pre-ATL-L, post-ATL-L and ATL-L groups. Three sets of statistical analyses of these data, using repeated-measures ANOVA in a similar fashion to that reported above for the visible target trials, were completed in order to test these predictions

Table 5.

Descriptive Statistics for CG Arena Path Length: First four invisible target trials

	Trial 1	Trial 2	Trial 3	Trial 4
Pre-ATL-R (*n* = 7)	304.45 (188.78)	425.69 (211.14)	364.24 (179.73)	393.39 (228.99)
Pre-ATL-L (*n* = 5)	457.56 (258.56)	526.92 (230.29)	216.97 (145.36)	244.74 (204.90)
Post-ATL-R (*n* = 6)	362.53 (75.10)	325.89 (200.32)	322.53 (169.82)	166.19 (117.62)
Post-ATL-L (*n* = 10)	365.83 (201.99)	265.83 (165.39)	143.28 (74.19)	148.68 (36.13)
ATL-R (*n* = 13)	331.26 (145.18)	379.63 (204.19)	344.99 (169.22)	288.49 (214.22)
ATL-L (*n* = 15)	396.41 (217.56)	352.61 (221.39)	167.84 (104.22)	180.70 (122.61)
Control (*n* = 30)	386.09 (258.50)	166.21 (105.03)	132.31 (127.69)	104.97 (54.82)

Note. Means are presented with standard deviations in parentheses.

Table 6.

Descriptive Statistics for CG Arena Path Length: Final four invisible target trials

	Trial 5	Trial 6	Trial 7	Trial 8
Pre-ATL-R (*n* = 7)	377.71 (255.95)	65.31 (58.7)	249.4 (188.93)	203.67 (134.62)
Pre-ATL-L (*n* = 5)	125.89 (120.34)	109.14 (90.55)	100.71 (37.54)	109.84 (41.74)
Post-ATL-R (*n* = 6)	129.97 (84.27)	257.28 (149.31)	143.17 (55.13)	184.60 (111.15)
Post-ATL-L (*n* = 10)	99.03 (80.7)	32.25 (12.75)	97.68 (39.7)	123.35 (45.47)
ATL-R (*n* = 13)	241.83 (217.56)	153.91 (144.68)	200.37 (148.83)	194.87 (119.61)
ATL-L (*n* = 15)	107.98 (92.17)	57.88 (62.09)	98.69 (37.66)	118.85 (43.25)
Control (*n* = 30)	50.38 (33.66)	57.77 (53.77)	97.63 (48.66)	89.49 (45.10)

Note. Means are presented with standard deviations in parentheses.

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of trials, $\chi^2(27) = 121.97$, $p < .001$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .513$). Within-subjects comparisons revealed a statistically significant main effect of trials on path length to target, $F(3.590, 140.016) = 18.137$, $p < .001$. The interaction effect of trials x group was also statistically significant, $F(7.18, 140.016) = 4.782$, $p < .001$, as was the main effect of group, $F(2, 39) = 21.151$, $p < .001$.

Multiple comparisons using the Games-Howell calculation revealed a statistically significant difference between the pre-ATL-R and control groups ($p = .015$). Differences between the pre-ATL-L group and control group were not statistically significant ($p = .060$); neither were differences between the pre-ATL-L and pre-ATL-R groups ($p = .516$). Homogenous subsets,

using Tukey's Honestly Significant Difference (HSD) were formed, with the pre-ATL-L group and the pre-ATL-R group forming one subset and the control group another.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of trials, $\chi^2(27) = 170.09$, $p < .001$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .425$). Regarding within-subjects comparisons, the main effect of trials on path length to target was statistically significant, $F(2.974, 127.894) = 21.192$, $p < .001$. The interaction effect of trials x group was not statistically significant, $F(5.949, 127.894) = 1.708$, $p = .125$, but there was a statistically significant main effect of group, $F(2, 43) = 12.532$, $p < .001$.

Games-Howell multiple comparisons showed significant differences between the post-ATL-R and post-ATL-L groups ($p = .002$), as well as between the post-ATL-R and control groups ($p < .001$). No significant differences were found between the post-ATL-L and control groups ($p = .331$). Homogenous subsets, using Tukey's HSD, revealed two distinct groups. The control group and the post-ATL-L group formed one subset and the post-ATL-R group was alone in the other subset.

The third set of analyses compared the performance of the entire ATL-R group, the entire ATL-L group, and the control group. Again, Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of trials, $\chi^2(27) = 124.02$, $p < .001$. Therefore, degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\epsilon = .628$). Regarding within-subjects comparisons, a significant main effect of trials on path length to target was observed, $F(4.394, 241.689) = 28.868$, $p < .001$. The interaction effect of trials x group and the main effect of groups were also statistically significant, $F(8.789, 241.689) = 3.131$, $p = .002$, and $F(2, 55) = 21.502$, $p <. 001$, respectively.

Multiple post-hoc comparisons were conducted between the ATL-R, ATL-L and control groups. According to the Games-Howell calculation, all three groups differed significantly from one another. The ATL-R group differed significantly from the ATL-L group ($p = .019$) and from the

control group ($p < .001$); and the ATL-L group differed significantly from the control group ($p = .035$).

In summary, the main *a priori* prediction for performance of these participants on the CG Arena invisible target trials were largely confirmed: Participants with seizure focus in the right anterior temporal lobe and/or surgically placed lesions to the right anterior temporal lobe showed significantly worse performance on this task of spatial navigation than participants in the control group. The prediction that participants with seizure focus in the right anterior temporal lobe and/or surgically placed lesions to the right anterior temporal lobe would also perform more poorly than participants with seizure focus in the left anterior temporal lobe and/or surgically placed lesions to the left anterior temporal lobe was only partially confirmed, however: The post-ATL versus control and combined ATL versus control comparisons showed between-groups statistical significance in the predicted directions, but the pre-ATL versus control condition comparison suggested that both pre-ATL-R and pre-ATL-L participants performed worse than control group participants.

CG Arena: Probe trial

As noted earlier, in the 8 invisible-target trials preceding this probe trial, the target was hidden in a fixed location in the south-west quadrant of the arena. For the probe trial, the target was removed from the VE without the participant's knowledge. The dependent variable of interest here is, therefore, how long the participant spends searching that quadrant during the probe trial. This variable is referred to as "dwell time", and it is commonly used an indication of the robustness of a participant's cognitive map in spatial navigation tasks (Morris, 1984; Jacobs et al., 1997). Mean values for that dependent variable, for the pre-R-ATL, pre-L-ATL, post-R-ATL, post-L-ATL, ATL-R, ATL-L and control groups, are presented in Table 7.

The predictions for this outcome variable were identical to those made for the invisible target trials: participants in the pre-ATL-R group would perform worse (i.e., have a significantly shorter dwell time, and thus, it is assumed, a less robust cognitive map of the CG Arena) than those in the pre-ATL-L group; that participants in the post-ATL-R group would perform worse than those in the post-ATL-L group; and that participants in the ATL-R group would perform

worse than those in the ATL-L group. Furthermore, it was predicted that participants in the control group would perform significantly better than those in the pre-ATL-R, post-ATL-R, and ATL-R groups, but would perform similarly to participants in the pre-ATL-L, post-ATL-L and ATL-L groups. Figure 3 is a graphical representation of performance on the CG Arena probe trial. From this figure, it is clear that these predictions were confirmed. One-way ANOVAs were used to test these predictions.

Table 7.
Descriptive Statistics for CG Arena Probe Trial, ORT, and ART Performance

	Probe Trial Dwell Time	ORT *d'*	ART score
Pre-ATL-R (*n* = 7)	20.62 (14.13)	1.09 (0.74)	4.14 (1.57)
Pre-ATL-L (*n* = 5)	40.85 (8.49)	1.93 (0.95)	7.20 (1.48)
Post-ATL-R (*n* = 6)	31.69 (7.44)	1.72 (0.99)	3.83 (2.04)
Post-ATL-L (*n* = 10)	37.62 (4.00)	1.93 (0.89)	6.80 (1.81)
ATL-R (*n* = 13)	25.73 (12.49)	1.38 (0.89)	4.00 (1.73)
ATL-L (*n* = 15)	38.70 (5.78)	1.90 (0.88)	6.90 (1.67)
Control (*n* = 30)	41.72 (6.98)	1.96 (1.12)	7.60 (1.52)

Note. Means are presented with standard deviations in parentheses. ORT = Object Recognition Task; ART = Arena Reconstitution Task.

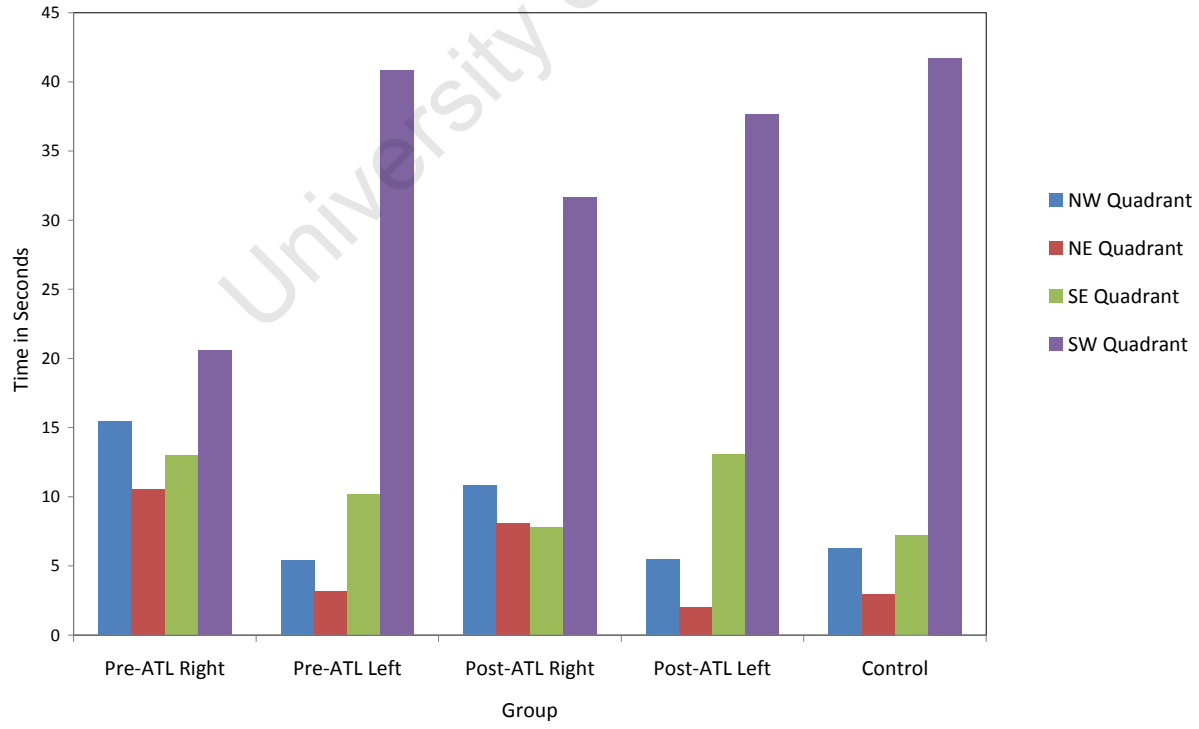

Figure 3. Performance on the CG Arena probe trial

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups. Levene's statistic was found to be significant, $p = .015$; therefore, the assumption of homogeneity of variance had been violated, and an adjusted F is reported here. Nonetheless, there were statistically significant between-group differences, Welch's $F(2, 7.495) = 6.78$, $p = .021$. The Games-Howell calculation of multiple comparisons was used to shed further light on the data. Statistically significant differences were found between the pre-ATL-R and pre-ATL-L groups ($p = .029$) and between the pre-ATL-R and control groups ($p = .017$). The difference between the pre-ATL-L and control groups was not statistically significant. Tukey's HSD homogenous subsets analysis separated the pre-ATL-R group, on the one hand, from the pre-ATL-L and control groups, on the other.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups. Levene's test was not significant, $p = .160$; therefore the assumption of homogeneity of variance was upheld. Again, a statistically significant between-groups difference was found, $F(2, 43) = 6.439$, $p = .004$. Tukey's HSD multiple comparisons revealed a statistically significant difference between the post-ATL-R and control groups ($p = .004$). No statistically significant differences were found between the post-ATL-L and control groups or the post-ATL-R and post-ATL-L groups. Tukey's HSD homogenous subsets revealed two homogenous groups. Group 1 included the post-ATL-R and post-ATL-L groups and group 2 included the post-ATL-L group and the control group.

The third set of analyses compared the performance of the ATL-R, ATL-L and control groups. Levene's test was significant, $p = .001$; therefore the assumption of homogeneity of variance had been violated, and an adjusted F is reported here. Again, a statistically significant between-groups difference was observed, Welch's $F(2, 25.258) = 9.31$, $p = .001$. The Games-Howell calculation was used to interpret the multiple comparisons. A significant difference was found between the ATL-R and ATL-L groups ($p = .009$) as well as between the ATL-R and control groups ($p = .002$). Differences between the ATL-L and control groups were found to be statistically non-significant ($p = .286$). Tukey's HSD homogenous subsets analysis separated the ATL-R group, on the one hand, from the ATL-L and control groups, on the other.

In summary, the results from these three sets of analyses are reasonably consistent, and serve to confirm the prediction that, on the measure of dwell time (an indication of the strength of a participant's cognitive map), participants with seizure focus in the right anterior temporal lobe and/or surgically placed lesions to the right anterior temporal lobe would (a) perform worse than control participants, and (b) perform worse than participants with seizure focus in the left anterior temporal lobe and/or surgically placed lesions to the left anterior temporal lobe. The prediction that there would be no statistically significant differences between the latter two groups of participants on this measure was also confirmed.

Object Recognition Task (ORT)

Descriptive statistics for the participants' ORT *d'* scores are shown in Table 7. Three simple one-way ANOVAs were conducted on these data to test the prediction that, because this task taps into simple recognition memory and not spatial memory (Thomas et al., 2003), all participants should perform similarly on this task.

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups. Levene's test was found to be non-significant ($p = .224$); therefore, the assumption of homogeneity of variance was upheld. As predicted, there were no statistically significant between-groups differences in recognition memory for pictures in the CG Arena experimental room, $F(2, 39) = 1.972$, $p = .153$.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups. Levene's test was found to be non-significant ($p = .568$); therefore the assumption of homogeneity of variance was upheld. Again, there were no statistically significant between-group differences in recognition memory for pictures in the CG Arena experimental room, $F(2, 43) = 0.129$, $p = .879$.

The third set of analyses compared the performance of the ATL-R, ATL-L and control groups. Levene's test was found to be non-significant ($p = .249$); therefore the assumption of homogeneity of variance was upheld. Once again, there were no statistically significant between-

group differences in recognition memory for pictures in the CG Arena experimental room, $F(2, 55) = 1.598$, $p = .211$.

In summary, the results from these three analyses are consistent, and serve to confirm the prediction that, on a measure of simple recognition memory, participants in all of the patient groups would perform similarly to one another and to participants in the control group.

Arena Reconstitution Task (ART)

Descriptive statistics for the participants' ART scores are shown in Table 7. Three simple one-way ANOVAs were conducted on these data to test the following set of predictions, which are based on the fact that task taps into spatial learning and memory abilities and is a good measure of the robustness of a participant's cognitive map (Thomas et al., 2003): (1) participants in the pre-ATL-R group would perform worse (i.e., have significantly lower ART scores, and thus, it is assumed, a less robust cognitive map of the CG Arena) than those in the pre-ATL-L group; (2) participants in the post-ATL-R group would perform worse than those in the post-ATL-L group; and (3) participants in the ATL-R group would perform worse than those in the ATL-L group. Furthermore, it was predicted that (4) participants in the control group would perform significantly better than those in the pre-ATL-R, post-ATL-R, and ATL-R groups, but would perform similarly to participants in the pre-ATL-L, post-ATL-L and ATL-L groups. One-way ANOVAs were used to test these predictions.

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L, and control groups. Levene's test was found to be non-significant, $p = .787$; therefore, the assumption of homogeneity of variance was upheld. There was a statistically significant between-groups difference in terms of the ability to reconstruct the spatial relationships of the pictures in the CG Arena experimental room, $F(2, 39) = 14.619$, $p < .001$. Tukey's HSD post-hoc tests revealed significant differences between the pre-ATL-R and pre-ATL-L groups ($p = .004$), and between the pre-ATL-R and control groups ($p < .001$). No statistically significant difference was found was observed between the pre-ATL-L and control groups ($p = .851$).

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L, and control groups. Levene's test was again found to be non-significant, $p = .818$; therefore, the assumption of homogeneity of variance was upheld. Again, there was a statistically significant between-groups difference in terms of the ability to reconstruct the spatial relationships of the pictures in the CG Arena experimental room, $F(2, 43) = 13.008$, $p < .001$. Tukey's HSD post-hoc tests revealed significant differences between the post-ATL-R and post-ATL-L groups ($p = .003$) and between the post-ATL-R and control groups ($p < .001$). No statistically significant difference was observed between the post-ATL-L and control groups ($p = .389$).

The third set of analyses compared the performance of the ATL-R, ATL-L, and control groups. Levene's test was again found to be non-significant ($p = .945$); therefore the assumption of homogeneity of variance was upheld. Again, there was a statistically significant between-groups difference in terms of the ability to reconstruct the spatial relationships of the pictures in the CG Arena experimental room, $F(2, 55) = 23.125$, $p < .001$. Tukey's HSD post-hoc tests revealed significant differences between the ATL-R and ATL-L groups ($p < .001$), and between the ATL-R and control groups ($p < .001$). No statistically significant difference was observed between the ATL-L and control groups ($p = .395$).

In summary, the results from these three sets of analyses are consistent, and serve to confirm the prediction that, on the ART, a measure of the strength of a participant's cognitive map, participants with seizure focus in the right anterior temporal lobe and/or surgically placed lesions to the right anterior temporal lobe would (a) perform worse than control participants, and (b) perform worse than participants with seizure focus in the left anterior temporal lobe and/or surgically placed lesions to the left anterior temporal lobe. The prediction that there would be no statistically significant differences between the latter two groups of participants on this measure was also confirmed.

Rey Complex Figure Test (RCFT)

Descriptive statistics for the participants' RCFT scores are shown in Table 8. The RCFT immediate and delayed recall tasks tap into visuospatial memory, and are a staple of the neuropsychological test batteries used in epilepsy centres and of studies into cognitive deficits

associated with temporal lobe epilepsy and temporal lobectomy (see, e.g., Graydon et al., 2001; Hermann & Wyler, 1988; Kilpatrick et al., 1997; Kneebone et al., 2007; McConley et al., 2008). As such, the predictions made here, and the manner in which those were tested, were identical to those made with regard to the CG Arena probe trial and the ART.

Table 8.
Descriptive Statistics for Performance on the Rey Complex Figure Test (RCFT)

Group	RCFT Immediate Recall	RCFT Delayed Recall
Pre-ATL-R (*n* = 7)	23.50 (2.34)	16.21 (2.18)
Pre-ATL-L (*n* = 5)	23.00 (2.26)	15.10 (2.61)
Post-ATL-R (*n* = 6)	23.58 (2.18)	14.67 (1.44)
Post-ATL-L (*n* = 10)	24.05 (2.42)	15.05 (2.35)
ATL-R (*n* = 13)	23.54 (2.17)	15.50 (1.97)
ATL-L (*n* = 15)	23.70 (2.34)	15.07 (2.34)
Control (*n* = 30)	24.98 (1.82)	16.05 (1.66)

Note. Mean scores are presented, with standard deviations in parentheses.

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups on the immediate and delayed recall trials. In each case, Levene's test was not statistically significant, $p = .411$ and $p = .280$, respectively; therefore, the assumption of homogeneity of variance was upheld for both one-way ANOVAs. A statistically significant between-group difference was found in terms of the ability to recall the complex figure after a short delay, $F(2, 39) = 3.289$, $p = .048$. However, after a longer delay, the result was found to be statistically non-significant $F(2, 39) = 0.63$, $p = .54$.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups on the immediate and delayed recall trials. In each case, Levene's test was not statistically significant, $p = 0.341$ and $p = .077$, respectively; therefore. The assumption of homogeneity of variance was upheld for both one-way ANOVAs. Again, there were no statistically significant between-group differences in terms of the ability to recall the complex figure after a short delay, $F(2, 43) = 1.698$, $p = .195$, and after a longer delay, $F(2, 43) = 2.185$, $p = .124$.

The third set of analyses compared performance of the ATL-R, ATL-L, and control groups on the immediate and delayed recall trials. In each case, Levene's test was not statistically significant, $p = .321$ and $p = .096$, respectively; therefore the assumption of homogeneity of variance was upheld for both one-way ANOVAs. Although there were statistically significant between-group differences in terms of the ability to recall the complex figure after a short delay, $F(2, 55) = 3.218$, $p = .048$, Tukey's HSD pairwise post-hoc tests detected no statistically significant differences. There were no statistically significant between-group differences in terms of the ability to recall the complex figure after a longer delay, $F(2, 55) = 1.377$, $p = .261$.

In summary, the results from these three sets of analyses are consistent, and serve to disconfirm the prediction that, on the RCFT, a standard clinical measure of visuospatial memory, participants with seizure focus in the right anterior temporal lobe and/or surgically placed lesions to the right anterior temporal lobe would (a) perform worse than control participants, and (b) perform worse than participants with seizure focus in the left anterior temporal lobe and/or surgically placed lesions to the left anterior temporal lobe. The prediction that there would be no statistically significant differences between the latter two groups of participants on this measure was confirmed, however.

Nine-Box Maze Test (NBMT)

Mean scores and standard deviations for the participants' NMBT scores are presented in Table 9. It should be noted here that this task was only administered to the post-surgical and control groups as it was not part of the standard neuropsychological test battery administered at the epilepsy clinic.

Table 9.
Descriptive Statistics and ANOVA Results for Performance on the NBMT

	Group				
Outcome variable	Post-ATL-R (n = 6)	Post-ATL-L (n = 10)	Control (n = 30)	F	p
O-W memory	5.10 (1.16)	5.70 (1.16)	3.20 (1.14)	20.88	< .001***
O-R memory	4.30 (1.37)	4.60 (0.97)	1.90 (0.9)	37.89	< .001***
S-W memory	6.50 (1.23)	4.20 (1.14)	4.20 (0.96)	12.93	< .001***
S-R memory	4.80 (0.98)	3.20 (0.63)	2.90 (0.89)	12.91	< .001***

Note. Mean scores are presented, with standard deviations in parentheses. O-W memory = object-working memory; O-R memory = object-reference memory; S-W memory = spatial-working memory; S-R memory = spatial-reference memory. Degrees of freedom for each between-group comparison were (2, 43).
*** $p < .001$

NBMT scores represent the number of errors made by the participant on the various tasks contained within the test. Therefore, a low score indicates fewer errors (and thus better performance) than a high score. The major prediction here was that participants in the post-ATL-R group would perform more poorly on the spatial memory measures of this task than participants in the post-ATL-L and control groups. It was further predicted that the post-ATL-L group would perform similarly to that of the control group on spatial memory measures.

The descriptive statistics shown in Table 9 suggest that participants in the post-ATL-L group and the post-ATL-R group scored similarly on the object-working and object-reference memory measures, while participants in the control group made fewer errors than participants in both of the patient groups on those measures. With regard to the spatial-working and spatial-reference memory measures, the post-ATL-L group preformed similarly to the control group. This is what one would expect to find because the post-ATL-L and control groups should not show spatial memory deficits. The post-ATL-R group made considerably more errors on both of these memory measures (spatial-working and spatial-reference) than the post-ATL-L and control groups. Figure 4 illustrates these findings.

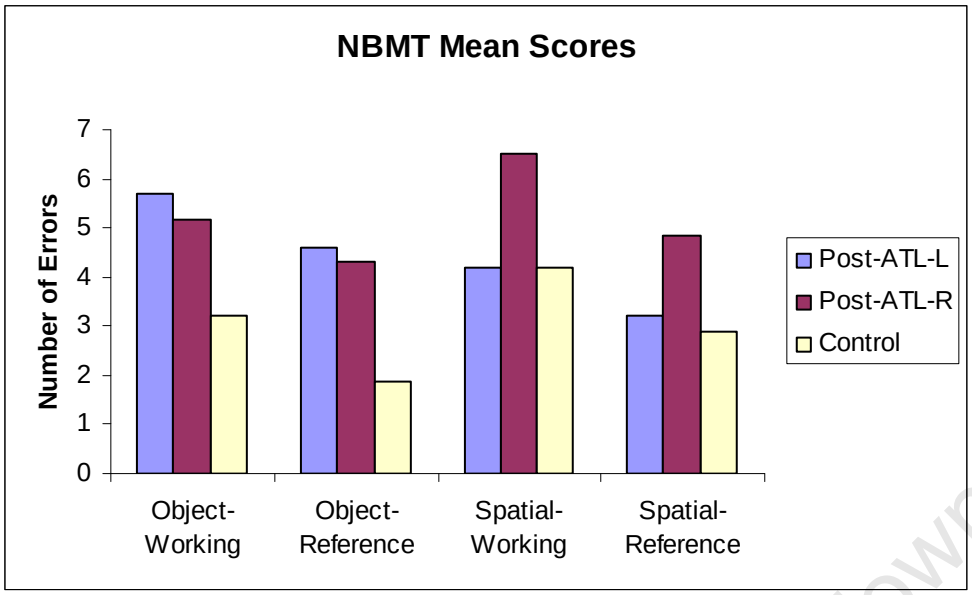

Figure 4. Mean scores for the NBMT in the three participant groups.

A series of simple one-way ANOVAs were conducted to test the NBMT predictions. For all of the ANOVAs, Levene's test was not statistically significant, indicating that the assumption of homogeneity of variance had not been violated. The results of the ANOVAs are presented in Table 9. As can be seen, statistically significant between-group differences were found on all four of the NBMT measures.

Tukey's HSD post-hoc comparisons were conducted in order to locate exactly where the between-group differences were. As can be seen from Table 10, for the object-working and object-reference memory measures, there were statistically significant differences between (a) the post-ATL-R and control groups, and (b) the post-ATL-L and control groups, but not (c) the post-ATL-R and post-ATL-L groups. For the spatial-working and spatial-reference memory measures, there were significant differences between (a) the post-ATL-R and control groups, and (b) the post-ATL-R and post-ATL-L groups, but not (c) the post-ATL-L and control groups. Therefore, the predictions were confirmed: On measures of non-spatial memory, the patients (regardless of laterality of lesion) performed more poorly than the controls, whereas on measures of spatial memory, the patients with surgically placed lesions to the right anterior temporal lobe performed more poorly than both the controls and the patients with surgically placed lesions to the left anterior temporal lobe.

Table 10.
Tukey's HSD Post-Hoc Test Results for NBMT Comparisons

	Outcome variable			
Comparison	Object-Working	Object-Reference	Spatial-Working	Spatial-Reference
1	$p = .64$	$p = .85$	$p < .001$***	$p = .002$**
2	$p = .002$**	$p < .001$***	$p < .001$***	$p < .001$***
3	$p < .001$***	$p < .001$***	$p = 1.00$	$p = .602$

Note. Comparison 1 = Post-ATL-R versus Post-ATL-L; Comparison 2 = Post-ATL-R versus Control; Comparison 3 = Post-ATL-L versus Control.
*$p < .05$, **$p < .01$, ***$p < .001$.

Summary: Spatial Cognition

In general, participants performed as predicted on tests of spatial navigation and related cognitive mapping skills. On the CG Arena visible target trials (a navigation test with no large spatial component) and the ORT (a recognition memory test with no large spatial component), no statistically significant between-group differences were found. In contrast, on the tests of navigation that featured large spatial component (the CG Arena invisible target trials, the CG Arena probe trial, and the ART), statistically significant between-group differences were found. These differences, as predicted, emerged from the significantly weaker performance of participants with right hemisphere temporal lobe epilepsy/right anterior temporal lobectomy. Small performance differences were occasionally observed between participants with left hemisphere temporal lobe epilepsy/left anterior temporal lobectomy and control participants, but for the most part participants in these two groups performed similarly.

On the standard clinical measure of visuospatial memory (the RCFT), there were no statistically significant between-groups differences on either immediate or delayed recall trials. This result is consistent with previous epilepsy studies (see, e.g., Kortenkamp, 2001; Kneebone et al., 2007; McConley et al., 2008), and confirms the typical experience of neuropsychologists working in epilepsy clinics.

The NBMT, as expected, revealed that the post-ATL-R group made more errors on the spatial memory measures of the task than the post-ATL-L and control groups and that there was no significant difference found between the post-ATL-L and control groups, indicating that these

two groups performed similarly. No significant differences were observed on the object memory measures when comparing post-ATL-R and post-ATL-L groups. However, both these groups differed significantly from the control group, indicating that these two groups performed similarly to each other, but both groups scored more errors than controls.

Verbal Memory

Descriptive statistics for all participants on all measures of verbal memory are presented in Table 11. For all of the listed dependent variables, the predictions here were that (1) participants in the pre-ATL-L group would perform more poorly than those in the pre-ATL-R group; (2) participants in the post-ATL-L group would perform more poorly than those in the post-ATL-R group; and (3) participants in the ATL-L group would perform more poorly than those in the ATL-L group. Furthermore, it was predicted that (4) participants in the control group would perform significantly better than those in the pre-ATL-L, post-ATL-L, and ATL-L groups, but would perform similarly to participants in the pre-ATL-R, post-ATL-R and ATL-R groups. A series of simple one-way ANOVAs were used to test these predictions.

WMS-III: Logical Memory

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups on the LM-I and LM-II tests. In each case, Levene's test was not statistically significant, $p = .198$ and $p = .147$, respectively; therefore, the assumption of homogeneity of variance was upheld for both one-way ANOVAs. There were statistically significant between-groups differences on both LM-I and LM-II, $F(2, 39) = 6.378$, $p = .004$, and $F(2, 39) = 12.688$, $p = .004$, respectively. Tukey's HSD post-hoc comparisons revealed significant differences between (a) the pre-ATL-L and control groups ($p = .002$) on the immediate recall measure, and (b) the pre-ATL-L and pre-ATL-R groups ($p = .011$), as well as the pre-ATL-L and control groups ($p < .001$), on the delayed recall trial.

Table 11.
Descriptive Statistics for Performance on Tests of Verbal Memory

Test/ Outcome Measure	Group						
	Pre-ATL-R (*n* = 7)	Pre-ATL-L (*n* = 5)	Post-ATL-R (*n* = 6)	Post-ATL-L (*n* = 10)	ATL-R (*n* = 13)	ATL-L (*n* = 15)	Control (*n* = 30)
WMS-III							
LM-I	32.86(2.85)	27.00 (4.00)	31.50 (2.17)	28.00 (1.63)	32.23 (2.56)	27.67 (2.55)	34.30 (4.5)
LM-II	18.14 (1.35)	13.60 (2.97)	17.17 (1.72)	14.20 (1.32)	17.70 (1.55)	14.00 (1.93)	19.77 (2.69)
PAL-I	14.71 (2.56)	10.20 (1.48)	13.17 (1.47)	11.29 (1.64)	14.00 (2.20)	10.93 (1.62)	15.67 (2.45)
PAL-II	4.28 (1.11)	3.00 (0.71)	4.00 (1.41)	3.10 (0.99)	4.15 (1.21)	3.07 (0.88)	4.20 (0.93)
RAVLT							
Encoding	8.57 (2.64)	5.20 (1.92)	8.51 (1.38)	6.50 (1.08)	8.54 (2.07)	6.07 (1.49)	7.23 (1.30)
Acquisition	61.00 (6.27)	44.00 (11.94)	61.17 (4.49	53.60 (4.58)	61.08 (5.30)	50.40 (8.72)	60.40 (3.44)
STPR	96.00 (6.68)	77.00 (33.96)	93.17 (6.05)	88.39 (5.44)	94.70 (6.30)	84.60 (19.48)	97.17 (3.53)
LTPR	86.00 (10.06)	72.20 (32.57)	87.67 (4.89)	77.80 (5.49)	86.80 (7.83)	75.93 (18.16)	87.40 (7.30)
LOT	18.14 (7.06)	18.00 (5.24)	18.67 (4.55)	20.90 (3.07)	18.38 (5.80)	19.93 (3.99)	24.06 (4.07)

Note. Mean scores are presented, with standard deviations in parentheses. WMS-III = Wechsler Memory Scale-Third Revision; LM-I = Logical Memory I – Immediate Recall; LM-II = Logical Memory II – Delayed Recall; PAL -I = Paired Associates Learning I – Immediate Recall; PAL-II = Paired Associates Learning II – Delayed Recall; RAVLT = Rey Auditory-Verbal Learning Test; STPR = Short-Term Percent Retention; LTPR = Long-Term Percent Retention; LOT = Learning Over Trials.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups on the LM-I and LM-II tests. Levene's test was statistically significant for the both of these ANOVAs, $p = .001$ and $p = .036$, respectively; therefore, the assumption of homogeneity of variance was violated in both cases, and robust estimates of F were used. There were statistically significant between-groups differences on both LM-I and LM-II, Welch's $F(2, 15.711) = 21.64$, $p < .001$, and Welch's $F(2, 14.620) = 36.12$, $p < .001$, respectively. Tukey's HSD post-hoc comparisons revealed statistically significant differences between (a) the post-ATL-L and control groups ($p < .001$) on the immediate recall measure, and (b) the post-ATL-L and post-ATL-R groups ($p = .049$), the post-ATL-R and control groups ($p = .046$), and the post-ATL-L and control groups ($p < .001$) on the delayed recall trial.

The third set of analyses compared the performance of the ATL-R, ATL-L and control groups on the LM-II and LM-II tests. Levene's test was statistically significant for both ANOVAs, $p = .002$ and $p = .039$, respectively; therefore, the assumption of homogeneity of variance was violated in both cases, and robust estimates of F were used. There were statistically significant between-groups differences on both LM-I and LM-II, Welch's $F(2, 33.067) = 21.88$, $p < .001$, and Welch's $F(2, 32.454) = 34.31$, $p < .001$, respectively. Tukey's HSD post-hoc comparisons revealed statistically significant differences between (a) the ATL-L and ATL-R groups ($p = .006$), as well as the ATL-L and control groups ($p < .001$) on the immediate recall measure, and (b) the ATL-L and ATL-R groups ($p < .001$), the ATL-R and control groups ($p = .023$), and the ATL-L and control groups ($p < .001$) on the delayed recall trial.

WMS-III: Paired Associates Learning

The first set of analyses compared the performance of the pre-ATL-R, pre-ATL-L and control groups on the PAL-I and PAL-II tests. In each case, Levene's test was not statistically significant, $p = .237$ and $p = .301$, respectively; therefore, the assumption of homogeneity of variance was upheld for both one-way ANOVAs. There were statistically significant between-groups differences on both PAL-I and PAL-II, $F(2, 39) = 11.219$, $p < .001$, and $F(2, 39) = 3.735$, $p = .033$, respectively. Tukey's HSD post-hoc comparisons

revealed significant differences between (a) the pre-ATL-L and control groups ($p < .001$), as well as the pre-ATL-L and pre-ATL-R groups ($p = .007$) on the immediate recall measure, and (b) the pre-ATL-L and control groups ($p = .030$) on the delayed recall trial.

The second set of analyses compared the performance of the post-ATL-R, post-ATL-L and control groups on the PAL-I and PAL-II tests. In each case, Levene's test was not statistically significant, $p = .062$ and $p = .616$, respectively; therefore, the assumption of homogeneity of variance was upheld for both one-way ANOVAs. There were statistically significant between-groups differences on both PAL-I and PAL-II, $F(2, 43) = 15.731$, $p < .001$, and $F(2, 43) = 4.497$, $p = .017$, respectively. Tukey's HSD post-hoc comparisons revealed significant differences between (a) the post-ATL-L and control groups ($p < .001$), as well as the post-ATL-R and control groups ($p = .039$) on the immediate recall measure, and (b) the pre-ATL-L and control groups ($p = .013$) on the delayed recall trial.

The third set of analyses compared the performance of the ATL-R, ATL-L and control groups on the PAL-I and PAL-II tests. In each case, Levene's test was not statistically significant, $p = .083$ and $p = .336$, respectively; therefore, the assumption of homogeneity of variance was upheld for both one-way ANOVAs. There were statistically significant between-groups differences on both PAL-I and PAL-II, $F(2, 55) = 22.861$, $p < .001$, and $F(2, 55) = 7.182$, $p = .002$, respectively. Tukey's HSD post-hoc comparisons revealed significant differences between (a) the ATL-L and control groups ($p = .002$), as well as the ATL-L and ATL-R groups ($p = .002$), on the immediate recall measure, and (b) the ATL-L and control groups ($p = .002$), as well the ATL-L and ATL-R groups ($p = .014$), on the delayed recall trial.

Rey Auditory-Verbal Learning Test (RAVLT)

The predictions were confirmed for most of this test's outcome measures: participants with left hemisphere temporal lobe epilepsy or surgically placed lesions to the left anterior temporal lobe performed more poorly than both (a) participants with right hemisphere temporal lobe epilepsy or surgically placed lesions to the right anterior

temporal lobe and (b) control participants. Participants in the latter groups generally performed similarly on these measures.

Summary: Tests of Verbal Memory

In general, participants performed as expected on tests of verbal memory, and predictions regarding these tasks were confirmed. As expected, on the WMS-III Logical Memory and Paired Associates Learning subtests, between-group differences were mostly observed between patients with right-sided damage and patients with left-sided damage, with the latter consistently performing more poorly on these tasks; as well as between patients with left-sided damage and normal controls. Little or no differences were observed between control participants and patients with right-sided damage.

Similar results were observed on the RAVLT; that is, generally speaking, patients with left-sided damage performed worse than both patients with right-sided damage and control participants. The only outcome variable that displayed an unexpected result was Learning Over Trials. On this outcome variable, the post-surgical group revealed significant differences between the control participants and the patients with right-sided damage, which is contrary to what one would expect to find. This finding will be discussed in more detail below.

The Effect of Exercise on Neuropsychological Functioning

The prediction here is that patients with active lifestyles (regardless of laterality of lesion) would perform better on all measures of neuropsychological functioning than patients with sedentary lifestyles (regardless of laterality of lesion). This prediction is based on the premise that exercise reduces the likelihood of seizure development, thereby reducing the associated hippocampal damage and consequent cognitive impairment associated with seizure.

In testing this prediction, pre- and post-surgical patient groups were combined in order to increase the sample size, thereby increasing statistical power and allowing for wider generalization of results. Left TLE/ATL and right TLE/ATL patient groups were kept separate, however, in order to minimize, in this analysis, the effect that laterality of lesion has on neuropsychological functioning (as it was shown to have in the above results). Means and standard deviations for the entire ATL-R and the entire ATL-L groups are represented in Tables 12 and 13. As can be seen, within each patient group the participants have been divided into "active" and "sedentary" categories. Those classed as active were individuals with a moderate to high levels of physical activity, as measured by the GPAQ questionnaire. Those classed as sedentary were individuals with low levels of physical activity, as measured by the GPAQ questionnaire.

The effect of exercise on neuropsychological test scores in active versus sedentary participants, within the ATL-R and ATL-L groups, was examined using simple one-way ANOVAs. For each of these analyses, Levene's test statistic was not statistically significant, and therefore the assumption of homogeneity of variance was upheld in all cases.

The first set of analyses compared the performance of active versus sedentary ATL-R patients; results from these analyses are shown in Table 13. Given that the CG Arena probe trial, ORT and ART results were in the expected directions in the above analyses, it was decided that these data would be sufficiently representative of the spatial navigation and cognitive mapping tasks; therefore these are the only CG Arena scores that were used in the present analyses. As Table 11 shows, the prediction that participants with active lifestyles would perform better than those with sedentary lifestyles was confirmed for all measures except WMS-III Logical Memory immediate recall, WMS-III Paired Associates Learning immediate recall, and the RAVLT.

The second set of analyses compared the performance of active versus sedentary ATL-L patients; results from these analyses are shown in Table 14. As the table shows, the prediction that participants with active lifestyles would perform better than those with

sedentary lifestyles was only confirmed for these measures: CG Arena probe trial, ART, RCFT immediate and delayed recall, and NMBT object-working, object-reference, and spatial-reference memory.

Table 12.
Descriptive Statistics and ANOVA Results for the Effect of Physical Activity Levels on Neuropsychological Functioning in ATL-R Participants

	ATL-R (n = 13)			
Test	Active (n = 7)	Sedentary (n = 6)	F	p
CG Arena				
Probe trial	35.09 (5.69)	14.80 (8.3)	27.000	< .001***
ORT	1.90 (0.82)	0.77 (0.51)	8.498	.014*
ART	5.29 (1.11)	2.50 (0.84)	25.235	< .001***
RCFT				
Immediate Recall	25.21 (1.19)	21.58 (1.07)	33.143	< .001***
Delayed Recall	16.71 (1.65)	14.08 (1.24)	10.192	.009**
NBMT[a]				
Object-Working	4.50 (0.58)	6.50 (0.71)	14.222	.019*
Object-Reference	3.50 (0.58)	6.00 (0.00)	33.333	.005**
Spatial-Working	5.70 (0.50)	7.50 (0.71)	13.067	.022*
Spatial-Reference	4.25 (0.50)	6.00 (0.00)	21.778	.009*
WMS-III				
LM I	33.29 (2.49)	31.00 (2.19)	3.023	.109
LM II	18.57 (1.27)	16.67 (1.21)	7.563	.019*
PAL I	15.00 (2.31)	12.83 (1.47)	3.895	.074
PAL II	5.00 (0.82)	3.17 (0.75)	17.480	.002**
RAVLT				
Encoding	9.14 (2.41)	7.83 (1.47)	1.334	.273
Acquisition	62.43 (6.53)	59.50 (3.27)	0.986	.342
STPR	93.14 (5.50)	96.50 (7.18)	0.910	.361
LTPR	87.14 (8.36)	86.33 (7.94)	0.032	.862
LOT	16.71 (6.34)	20.33 (4.89)	1.290	.280

Note. Mean scores are presented, with standard deviations in parentheses. Degrees of freedom for all between-group comparisons were (1, 11) unless otherwise noted.
[a]Statistics and analyses here are based on n = 4 in the Active group and n = 2 in the Sedentary group because the NBMT was only administered to post-ATL patients. In the case of the NBMT between-group comparisons, then, degrees of freedom were (1, 4).
*p < .05, **p < .01, ***p < .001.

Table 13.
Descriptive Statistics and ANOVA Results for the Effect of Physical Activity Levels on Neuropsychological Functioning in ATL-L Participants

	ATL-L (n = 15)			
Test	Active (n = 8)	Sedentary (n = 7)	F	p
CG Arena				
Probe trial	42.04 (5.41)	34.88 (3.44)	9.004	.010*
ORT	2.17 (0.82)	1.66 (0.92)	1.252	.283
ART	7.88 (1.13)	5.86 (1.57)	8.327	.013*
RCFT				
Immediate Recall	24.94 (2.31)	22.29 (1.49)	6.738	.022*
Delayed Recall	16.56 (2.06)	13.36 (1.22)	12.926	.003**
NBMT[a]				
Object-Working	5.00 (0.63)	6.75 (0.96)	12.38	.008**
Object-Reference	4.00 (0.63)	5.50 (0.58)	14.40	.005**
Spatial-Working	4.17 (0.41)	4.25 (0.5)	.012	.092
Spatial-Reference	2.83 (0.41)	3.75 (0.5)	10.19	.013*
WMS-III				
LM I	28.00 (3.34)	27.29 (1.38)	0.277	.608
LM II	14.50 (2.45)	13.43 (0.98)	1.168	.299
PAL I	11.62 (1.77)	10.14 (1.07)	3.711	.076
PAL II	3.37 (0.92)	2.71 (0.76)	2.277	.155
RAVLT				
Encoding	6.25 (1.83)	5.86 (1.07)	0.247	.628
Acquisition	51.38 (11.55)	49.29 (4.39)	0.202	.660
STPR	81.38 (26.78)	88.29 (4.39)	0.451	.513
LTPR	72.13 (23.02)	80.29 (10.50)	0.739	.405
LOT	20.13 (3.36)	19.71 (4.89)	0.037	.851

Note. Mean scores are presented, with standard deviations in parentheses. Degrees of freedom for all between-group comparisons were (1, 13) unless otherwise noted.
[a]Statistics and analyses here are based on n = 6 in the Active group and n = 4 in the Sedentary group because the NBMT was only administered to post-ATL patients. In the case of the NBMT between-group comparisons, then, degrees of freedom were (1, 8).
*p < .05, **p < .01.
2

Discussion

Hypothesis 1: Spatial memory and navigation

Hypothesis 1 predicted that right TLE/right ATL patients would perform more poorly on tasks of spatial memory/navigation than left TLE/left ATL patients, and that the latter would perform similarly to healthy control participants. This prediction was largely confirmed by the results. These data are encouraging considering the vast body of literature that has failed to find an association between right-sided hippocampal damage and spatial memory deficits (Kilpatrick et al., 1997; Lee, Yip & Jones-Gotman, 2002; Wilde et al., 2001).

With regard to the CG Arena invisible target trials, as expected, within the post-surgical group and the overall patient group (i.e., both pre- and post-surgical participants), patients with right-sided hippocampal damage performed significantly more poorly than both (a) patients with left-sided hippocampal damage and (b) healthy control participants. However, two results obtained on this measure were not congruent with expectations.

First, in the pre-surgical group, it was found that patients with right-sided hippocampal damage performed similarly to patients with left-sided hippocampal damage and that both these groups performed more poorly than normal control participants. This result could be explained in terms of research conducted by Astur et al. (2002). In their study examining spatial memory impairments on a virtual Morris water task, they found that, in humans, impairments in spatial learning/memory occurred following unilateral hippocampal removal, but that these impairments occurred regardless of the side of damage. The authors concluded that performance in their navigational task is dependent upon bilateral involvement of the hippocampus. This notion could be plausible, considering the findings of the present study.

Second, in the overall patient group, while it was found that patients with right-sided hippocampal damage performed more poorly than patients with left-sided hippocampal

damage, it was also found that both these two groups performed more poorly than normal control participants. This is contrary to expectation as it was predicted that the patients with left-sided damage would perform similarly to healthy control participants. This could, once again in part, be explained by the findings of Astur et al. (2002). A further explanation for this could be that the slightly skewed results of the pre-surgical group resulted in a slightly skewed result for the combined ATL group. Perhaps results from the post-surgical group, where results confirmed the prediction, were more representative than those of the pre-surgical group.

With regard to the CG Arena probe trial, results also largely confirmed the prediction. In both the pre-surgical group and the overall patient group, it was found that patients with right-sided hippocampal damage performed more poorly than both (a) patients with left-sided hippocampal damage and (b) healthy control participants. In all three groups, patients with left-sided hippocampal damage generally performed similarly to control participants. The only result that did not fit with this prediction was found in the post-surgical group, where patients with right-sided hippocampal damage performed similarly to patients with left-sided hippocampal damage. While patients with right-sided hippocampal damage performed more poorly than normal control participants, which was expected, it seemed to be unclear whether patients with left-sided hippocampal damage performed more similarly to controls or patients with right-sided hippocampal damage. This result could again be explained in terms of the findings of Astur et al. (2002): Perhaps optimal spatial cognition/spatial navigation does indeed rely on both the right and left hippocampus.

In terms of the Arena Reconstitution Task, results were as predicted across all three groups. Patients with right-sided hippocampal damage performed more poorly than patients with left-sided hippocampal damage; the former performed more poorly than normal control participants and the patients with left-sided hippocampal damage performed similarly to normal control participants. These results confirmed the prediction indicating that an association exists between right hippocampus and spatial cognition and

that this task has good lateralizing value regarding left and right hippocampus and related material specificities.

With regard to the RCFT, no significant between-group differences were found. This result is consistent with previous research findings (e.g., Hermann et al., 1994; Kilpatrick et al., 1997; Miller et al., 1993). These authors suggest that this finding could be explained by the fact that the to-be-remembered figure can easily be verbally encoded by the patient, thereby allowing reliance on verbal memory related structures, rather than pure visuospatial related structures, for successful task completion. While this test is a widely used measure of visuospatial memory in studies into cognitive deficits associated with temporal lobe epilepsy and temporal lobectomy (see, e.g., Graydon et al., 2001; Hermann & Wyler, 1988; Kilpatrick et al., 1997; Kneebone et al., 2007; McConley et al., 2008) and is also the staple of the neuropsychological test batteries used in epilepsy centers, its use could be seen as one possible reason for the lack of empirical findings confirming the association between right hippocampus and spatial cognition.

With regard to the NBMT, results confirmed the prediction in that the participants in the post-ATL-R group performed more poorly than those in both the (a) post-ATL-L group and (b) healthy control group on the spatial memory measures of the task. On the object memory measure of the task, the patient groups performed similarly; more specifically, participants in both of these groups performed more poorly than those in the healthy control group. These results are consistent with those found by Abrahams et al. (1996). These authors found deficits on both spatial memory components of the NBMT in a TLE group and an ATL group with right-sided damage; in contrast, left TLE and left ATL participants performed similarly to control participants. Abrahams and colleagues also found that the right and left TLE/ATL participants performed similarly on the object memory components and that the participants in these groups made more errors on this task than did participants in a healthy control group. Their research, and therefore the present research, thus provides support for the cognitive mapping theory of hippocampal function of O'Keefe and Nadel (1978), rather than the working memory theory of Olton et al. (1979). The cognitive mapping theory suggests that the right hippocampus is

responsible for spatial memory, particularly allocentric processing of spatial memory (O'Keeke &Nadel, 1978). However, the working memory theory suggests that the hippocampus is responsible for processing information relevant to the present situation or context. This working memory is contrasted with reference memory which processes information that remains constant across situations (Olton, 1979).

These results are encouraging as they confirm and expand on the results of Abrahams et al. (1996). The present study also extends research conducted by Thomas et al. (2001). The authors evaluated two individuals who had experienced right temporal lobectomy for the relief of intractable epilepsy. Neither of these individuals had difficulty locating and navigating towards a visible target, but both displayed difficulty in consistently relocating an invisible target. The results of the present study have expanded and built upon these results and provided further evidence for the association between the right hippocampus and spatial cognition as well as the reliability of the CG Arena in detecting deficits in spatial cognition.

Hypothesis 2: Verbal learning and memory

Hypothesis 2 predicted that TLE/ATL patients with left-sided hippocampal damage would perform more poorly on tasks of verbal memory than patients with right-sided hippocampal damage and that the latter would perform similarly to healthy control participants. These predictions were largely confirmed. In terms of the WMS-III Logical Memory and Paired Associates Learning subtests, between-group differences were mostly observed between patients with right-sided hippocampal damage and patients with left-sided hippocampal damage, with the latter consistently performing more poorly on these tasks. Similar patterns of difference were observed between patients with left-sided hippocampal damage and normal controls. Few or no differences were observed between normal control participants and patients with right-sided hippocampal damage. These results are consistent with previous literature (Bell & Davies, 1998; Graydon, Nunn, Polkey & Morris, 2001; Lee, Yip & Jones-Gotman, 2002; Seidenberg et al., 1996;

Seidenberg et al., 1998) indicating a strong association between verbal memory and left hemisphere hippocampal functioning.

In terms of the RAVLT, predictions were largely confirmed. On most of the outcome variables, patients with left-sided hippocampal damage performed more poorly than those with right-sided hippocampal damage. One outcome variable, the Learning Over Trials outcome variable, produced a different result, however. On that outcome variable, significant differences were found between the post-surgical patients with right-sided damage and the healthy control participants. This piece of data is contrary to what one would expect to find, given the well-established association between left hippocampal damage and verbal memory decline. One study, however, does provide evidence of a similar unexpected link between right hippocampal damage and verbal memory. Peters et al. (2009) investigated verbal recognition memory in three patients with focal ischemic lesions to the right medial temporal lobe. Their study suggests that the right anterior hippocampus may also contribute to verbal recollection, similar to neuroimaging studies that have found a joint involvement of the left and right medial temporal lobe in verbal recollection.

Hypothesis 3: The effect of exercise on neuropsychological functioning

Hypothesis 3 predicted that active TLE/ATL patients would perform better than sedentary TLE/ATL patients on all measures of neuropsychological functioning. This prediction was only partially confirmed. With regard to tests of spatial cognition, as predicted, active patients performed better than sedentary patients in both left- and right-sided hippocampal damage groups. Therefore, an association between degree of hippocampal function, particularly spatial memory, and activity level has been established.

However, results obtained for verbal memory measures were not entirely as predicted. On all tests of verbal memory, active and sedentary patients performed similarly. This result is inconsistent with what one would expect to find, given that the positive effects of

exercise on hippocampal function should, in theory, be applicable to both left and right hippocampus. However, one previous study has reported similar findings. As mentioned in the Introduction, Stroth et al. (2008) examined the benefits of aerobic endurance exercise on memory and affect in young adults. Specifically the authors investigated whether three running sessions of 30 minutes per week over a 6-week period had the potential to improve visuospatial and verbal memory, concentration performance and affect in healthy young adults. Twenty-eight students participated in the study and were divided into an experimental group, who took part in the training program, and a control group, who were asked not to vary their everyday activities. Results from their study showed a significant increase in visuospatial memory performance and positive affect; however, no effects of running training were observed on concentration performance or verbal memory.

Similarly, Eriksen et al. (2009) investigated the association between aerobic fitness and hippocampal volume in elderly humans. The authors examined the magnetic resonance images of 165 non-demented older adults and found that higher fitness levels were associated with larger volumes in left and right hippocampi. It was also found that higher fitness levels were associated with better spatial memory than individuals with lower fitness levels.

In summary, the present study aimed to investigate verbal and spatial memory in ATL-L and ATL-R patients and whether activity levels of these patients had an effect on neuropsychological functioning. Furthermore, the present study tested epileptic adults on a task of spatial navigation which has proved to be more sensitive in detecting deficits than spatial memory tasks used in previous research. Overall, predictions were, more often than not, confirmed and results proved to be promising.

Previous research failed to consistently confirm the association between right hippocampus and spatial cognition. The present study aimed to address this issue and has, to a large extent, achieved this aim. While testing materials used in previous research proved to be inadequate, the present study used a navigational task in a virtual

environment as well as a desktop spatial memory task. These tasks both proved to be somewhat more sensitive to right hemisphere hippocampal function than previously used desktop tasks. A framework for research on this topic has been provided and can only serve for further research to build upon.

Limitations and directions for future research

Several limitations of the current study should be addressed by future researchers who wish to more clearly establish the association between right hippocampus and spatial cognition as well as the relationship between exercise and hippocampal function. Firstly, although some hypotheses were largely confirmed, those that were not completely confirmed may require larger sample sizes. Larger sample sizes will increase the generalisability of the results and therefore provide a more plausible framework from which to work.

Secondly, while the present study was cross-sectional in nature, future research would benefit from taking a longitudinal approach. Evaluating the same participants before and after surgery for intractable epilepsy may provide interesting results. Neuropsychological functioning can be evaluated both before and after surgical intervention in order to establish whether or not there is a decline, or an improvement, in cognition. Although numerous such studies have been completed (see e.g., Bell & Davies, 1998; Helmstaedter et al., 2007; Hermann & Wyler, 1988; Killgore et al., 1999; Shin et al., 2009), none have included a spatial navigational task such as the present study had done.

Thirdly, it is imperative that future studies examine MRI scans of all participants in order to establish the effects of the degree of hippocampal sclerosis on neuropsychological functioning. Bell and Davies (1998) state that the sole pathology found in approximately 80% of all pre-surgical ATL patients is hippocampal sclerosis (HS), which is often associated with an early brain injury. HS is characterized by neuronal loss, gliosis and atrophy. The degree of HS has a further effect on the neuropsychological outcome of ATL. Specifically, a patient with discrete HS is likely to display greater post-surgical

decline as a result of the part-removal of a functioning structure than a patient with moderate to marked HS.

Comprehensive fMRI studies will also be able to clearly establish the exact brain structures that relate to spatial cognition (see e.g., Abrahams et al., 1999; Hermann et al., 2002; Oyegbile et al., 2006; Vingerhoets et al., 2003). Whilst most of the literature focuses on the role of the hippocampus, there has been much debate around the role of the amygdala and the parahippocampal regions. While these areas of the brain are affected by epilepsy and portions of these regions are removed during an anterior temporal lobectomy, it is difficult to establish the role that each of these structures play in spatial cognition.

The role of the amygdala in spatial cognition was introduced by Pegna et al. (2002). The authors found a correlation between visuospatial memory performance and right amygdala, rather than right hippocampal volume and suggested that, contrary to expectations, the right amygdala (rather than the hippocampus) could play a significant role in retaining visuospatial information over a prolonged period of time. Based on their study, further research should be conducted on the role of amygdale in spatial memory as this aspect was not within the scope of the present study.

Fourth, the present study was not able to match participants with regard to age of seizure onset, seizure frequency and duration of disorder, seizure type, etiology and anti-epileptic drugs; however, these factors are important to consider. Previous research has indicated that these factors can also play a role in neuropsychological functioning and are important to consider for a number of reasons. Age at seizure onset is an important contributing factor in cognitive functioning. In the immature brain, the hippocampus is at risk of developing age specific functional and anatomic pathologies. For example, a patient with childhood-onset TLE may have reduced white matter volume and associated poorer cognitive status. On the other hand, it is suggested that these patients could have less chance of developing postepileptic surgery dysnomia. This could be due to possible intrahemispheric reorganization of language early in life which acts as a protective factor.

Furthermore, it is suggested that motor skills are not impaired in childhood-onset right frontal lobe epilepsy when compared to patients with a later age at onset with lesions in the same hemisphere. However, the same has not been proved for the left hemisphere. The authors also explain that seizure frequency is a difficult factor to study in isolation from other factors such as duration and severity of the epilepsy. However, evidence suggests that higher frequency and duration of temporal lobe epilepsy are associated with more severe hippocampal atrophy and cognitive deficiency. Similarly, the development of hippocampal sclerosis (HS) and atrophy in patients with chronic TLE has been correlated with seizure duration. Evidence suggests that the longer the duration of the intractable epilepsy, the more severe the deficits in psychometric intelligence (Motamedi & Meador, 2003).

Moreover, the type of seizures and etiology can play an important role in cognitive functioning. Different epilepsy syndromes have different effects on cognition. Depending on the location and nature of the neuropathology, certain aspects of cognition and behaviour can be affected in symptomatic epilepsies. Although a small stroke or tumor may not involve any significant cognitive impairment, seizures associated with lesions in the frontal lobes or limbic system may result in language memory or psychological disturbances (Aldenkamp & Arends, 2004; Jokeit & Martina, 2003; Thompson & Duncan, 2005; Motamedi & Meador, 2003.).

Fifth, future studies would benefit from the inclusion of an epileptic control sample in order to compare test results of surgical patients to those of non-surgical patients. While the present study did not include such a group, these results would be of interest in order to establish whether a cognitive difference exists between those individuals whose epilepsy is well controlled with medication and those whose is not.

Finally, with regards to the effects of exercise on neuropsychological functioning in epileptic adults, recruiting active participants proved to be a difficult task. Many individuals with epilepsy find it difficult to participate in physical activity because of the possibility of seizures, leading not only to injury, but also embarrassment. Arida et al.

(2003) evaluated physical exercise habits in Brazilian patients with epilepsy by assessing the degree to which a group of 100 individuals with epilepsy were involved in physical activity and leisure activities. A questionnaire was administered to participants in order to establish possible barriers to exercise participation, including general barriers as well as epilepsy-specific barriers. Under the general category, the top 3 barriers included ‘’no-one to exercise with’’ (37%), ‘’tiredness after exercise’’ (38%) and ‘’unsure how to begin and proceed with an exercise program’’ (59%) (Arida et al., 2003, p. 509). Under the epilepsy-specific category, the top 3 barriers included; ‘’fear of being embarrassed by a seizure while exercising’’ (45%), ‘’previously experienced a seizure during exercise’’ (16%), and ‘’know of other persons with epilepsy who have had seizures while exercising’’ (16%) (Arida, et al. 2003, pg 509). This study concluded that only 15% of the sample could be categorized as active. This is a rather low percentage, given that exercise may possibly benefit individuals with epilepsy.

Therefore, it is suggested that future studies include an intervention strategy such as an exercise program that participants could participate in over a period of time within groups, lead by qualified individuals. Neuropsychological evaluations should be administered pre- and post-intervention. Future studies should include such intervention strategies in order to fully establish the effects of exercise on neuropsychological functioning (see e. g., Eriksen et al., 1994; 2009; Masley et al., 2009; Nakken et al., 1990; Stroth et al., 2009;).

Conclusion

The present study has made a substantial contribution to the area of interest by providing some interesting results and suggestions for future research. Where previous studies have failed, this study has succeeded in proving that an association between right hippocampus and spatial cognition does exist and that new tests are constantly being developed in order to more clearly establish this association. This study has also established a link between activity levels and neuropsychological functioning within an epileptic population, a topic

which has been given somewhat limited attention until now. Further studies are needed in order to more clearly establish the causative factors within this link.

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Appendix A

Sociodemographic and Health Questionnaire

Office Use

Reference Number: |__| |__| |__|

Gender: |__||__||__||__||__||__| *Code:* |__||__|

Age: |__| |__|

Years of Education: |__| |__|

Population Group: |__||__||__||__||__||__||__||__| *Code:* |__||__|

Home Language: |__||__||__||__||__||__||__||__||__|

Age of Seizure Onset: |__||__|

Seizure Frequency: |__||__||__|/day |__||__||__|/month |__||__||__|/year

Duration of Disorder: |__||__|

Antiepileptic Medication: |__||__||__||__||__||__||__||__||__||__||__||__||__||__||__||__|

Appendix B

Informed Consent Sheet

Title of Study:

Allocentric and Egocentric Spatial Memory Following Anterior Temporal Lobectomy: A comparison between active and sedentary epileptic adults.

Principal Investigator and Contact Information

Kevin G. F. Thomas, Ph.D.
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What is the purpose of this study?

The purpose of this study is to gain a deeper understanding of the brain functions affected by epilepsy. We are investigating what types of memory problems may be associated with epilepsy; whether there is an overall decline in memory following surgery and whether it is possible that exercise can contribute to reduced seizure frequency and therefore fewer memory deficits.

What can participants expect?

Participants are required to take part in a number of memory tests. The session is expected to last between 60 and 120 minutes. The tests will consist of tests of spatial memory as well as tests of verbal memory. Spatial memory tests include a computer generated task, a nine-box maze test and a complex drawing. The verbal memory tasks consist of stories and word lists. These tests are fun and may seem like games. The participants must however try their best. It is also important to relax and feel comfortable.

What are the potential risks or benefits of participating in this study?

There are no potential risks involved in participating in this study, nor are there any benefits to the participant. Participants will not be remunerated for their participation.

Your consent for this study and withdrawal from this study

Your participation in this study is voluntary. You do not have to participate if you do not want to. This information sheet will be discussed with you before you participate in this study. If you understand this information sheet and agree to participate in this study, you will sign your name at the bottom of the sheet. Before consenting, you will be told that you can withdraw at any time. You do not have to give a reason for withdrawing.

Confidentiality

Your taking part in the study, all facts collected about you, and the results of the tests will be private and not available to anyone other than the researcher and research assistants. You will be identified only by your reference number, which is known only by you and the researcher. Your identity will not be disclosed in any publication or presentation of this study.

You have been informed about this study's purpose, procedures, potential benefits and risks. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time. You voluntarily consent to participate in this study and by doing so; you are allowing the researchers and research assistants' access to all information obtained during the study.

Name of Participant: _____

Signature: _____ Date: _____

Name of Researcher: _____

Signature: _____ Date: _____

Appendix C

ART SCORING SHEET

1. All 8 item icons used ____
2. Item 6 alone on a wall ____
3. Item 5 alone on a wall ____
4. Two of 1-7-8 together on a wall ____
5. Items 1-7-8 together on a wall ____
6. Items 1-7-8 in correct order on a wall ____
7. Two of 3-2-4 together on a wall ____
8. Items 3-2-4 together on a wall ____
9. Items 3-2-4 in correct order on a wall ____
10. Entire reconstruction correct ____

Appendix D: Global Physical Activity Questionnaire (GPAQ v2.0)

Questions		Response	Code
Activity at Work			
1	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate (like carrying or lifting heavy loads, digging or construction work) for at least10 minutes continuously?	Yes 1 No 2 *If No, go to P4*	P1
2	In a typical week, on how many days do you do vigorous intensity activities as part of your work?	Number of days |__|	P2
3	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : Minutes |__| : |__|	P3 (a-b)
4	Does your work involve moderate-intensity activity that involves small increases in breathing or heart rate (such as brisk walking or carrying or lifting light loads) for at least10 minutes continuously?	Yes 1 No 2 *If No, go to P7*	P4
5	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days |__|	P5
6	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : Minutes |__| : |__|	P6
Travel to and from places			
7	Do you walk or use a bicycle for at least 10 minutes continuously to get to and from places?	Yes 1 No 2 *If No, go to P10*	P7
8	In a typical week, on how many days do you walk or use a bicycle for at least 10 minutes continuously to get to and from places?	Number of Days: |__|	P8
9	How much time do you spend walking or using a bicycle for travel on a typical day?	Hours : Minutes |__| : |__|	P9 (a-b)
Recreational Activities			
10	Do you do any vigorous-intensity sports, fitness or recreational activities that cause large increases in breathing or heart rate (like running or football) for at least 10 minutes continuously?	Yes 1 No 2 *If No, go to P13*	P10

11	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational activities?	Number of Days: |__|	P11
12	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : Minutes |__| : |__|	P12 (a-b)
13	Do you do any moderate-intensity sports, fitness or recreational activities that cause large increases in breathing or heart rate (like brisk walking or swimming) for at least 10 minutes continuously?	Yes 1 No 2 *If No, go to P16*	P13
14	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational activities?	Number of Days: |__|	P14
15	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational activities on a typical day?	Hours : Minutes |__| : |__|	P15 (a-b)
Sedentary Behaviour			
16	How much time do you usually spend sitting or reclining on a typical day?	Hours : Minutes |__| : |__|	P16 (a-b)