ACCELERATED LONG-TERM FORGETTING IN TEMPORAL LOBE EPILEPSY: TEST DEVELOPMENT, A GROUP COMPARISON AND CASE SERIES ANALYSIS

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DECLARATION

This thesis is submitted for a Doctorate in Clinical Psychology at the University of Sheffield. It has not been submitted for any other qualification or to any other institution.

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STRUCTURE AND WORD COUNTS

The literature review has been prepared in accordance with guidelines for authors submitting articles to Clinical Psychology Review. The research report has been prepared in accordance with guidelines for authors submitting articles to Epilepsia. Copies of the submission guidance for each journal and a letter approving the journal nominations are included in Appendix A.

Literature Review:

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MAIN ABSTRACT

This thesis examines accelerated long-term forgetting (ALF) in temporal lobe epilepsy (TLE). ALF refers to abnormal forgetting over hours to weeks in the absence of problems with acquisition or initial consolidation of memories. Currently ALF may go undetected since standardised assessments of memory only test at delays of up to 30-minutes. Since patients affected by ALF can experience considerable distress, the development of appropriate tests is essential to enable clinicians to assess this pattern of forgetting and understand whether it represents a distinct phenomenon.

Existing results regarding ALF are inconclusive and this may be due to methodological problems. A literature review summaries the methodological issues associated with assessing forgetting rates and evaluates whether existing studies have considered key issues. It is concluded that future studies would benefit from employing more rigorous methodology which includes both verbal and visual tests combining recall and recognition paradigms. It is also recommended that groups are well matched for age and IQ, initial learning is equated, ceiling and floor effects are avoided, rehearsal is minimised and immediate delays are long enough to ensure information has been stored in long-term memory.

A research study is then reported which combines individual and group analysis to examine the existence of ALF in TLE using specifically developed tests. Results demonstrate that when assessed using improved methodology, some people with TLE show ALF, some show forgetting over short delays and some have intact memory. It is concluded that there is considerable individual variation in the forgetting profiles of people with TLE highlighting that the reasons for this should be the focus of future research.

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ABSTRACT

Accelerated long-term forgetting (ALF) refers to abnormal forgetting over hours to weeks in the absence of problems with acquisition or initial consolidation; a phenomenon which has come under study in relation to epilepsy. Given that standardised assessments of memory typically only test at delays of up to 30-minutes, ALF may go undetected in clinical practise. Since patients affected by ALF can experience considerable distress, there is a clear need for clinicians to be able to assess this pattern of forgetting and understand whether it represents a distinct phenomenon.

Recent reviews examining ALF in patients with epilepsy have highlighted mixed results (with some showing ALF and some not) and suggested that methodological difficulties may be one reason for the inconsistencies. This review focuses specifically on methodological issues associated with assessing forgetting rates and evaluates the extent to which existing studies have considered key issues.

Future studies would benefit from more rigorous experimental designs to increase their comparability and validity. A range of verbal and visual tests should be piloted to identify which offer the most reliable measure of forgetting over long delays. In doing so, the goal of producing repeatable standardised tests for use in clinical practise should be upheld.

Key words: Accelerated long-term forgetting, forgetting rates, epilepsy, experimental design

INTRODUCTION

Memory impairments are common amongst people with epilepsy. 'Epilepsy' encompasses a range of neurological conditions which are hallmarked by the presence of seizures arising from abnormal electrical activity in the brain which can impact on behaviour and perception (Lezak, 2004). Temporal lobe epilepsy (TLE) is characterised by seizures originating from the temporal lobe region of the brain (Commission on Classification and Terminology of the International League Against Epilepsy, 1989). Studies have shown memory deficits are pronounced in TLE reflecting the degree of medial temporal lobe pathology associated with this disorder and the importance of the medial temporal lobes for memory (Helmstaedter, Grunwald, Lehnertz, Gleiβner, & Elger, 1997). It has been found that laterality of seizure focus influences the type of material for which memory is most affected. More specifically, seizures arising in the left temporal lobe tend to cause more pronounced deficits in verbal memory and (although less consistently), seizures arising in the right temporal lobe have a more marked affect on non-verbal memory (e.g. Butler and Zeman, 2008).

In attempting to better understand the memory impairments faced by people with epilepsy, attention has focused on a novel pattern of forgetting termed accelerated long-term forgetting (ALF). This term encompasses the phenomenon whereby initial learning and retention over delays of up to 30-minutes is intact, followed by unusually rapid forgetting over the following days to weeks. Of note, some studies have adopted the phrase long-term amnesia (Kapur et al., 1997, 1996; Mayes et al., 2003), however for clarity, only ALF will be used hereafter. As Butler and Zeman (2008) point out, this term distinguishes the disorder from amnesia which refers to a partial or total loss of memory most commonly caused by brain injury.

Anecdotal reports indicate that experiencing ALF can have a serious impact on quality of life, particularly when people report forgetting important episodic events such as family holidays or their wedding. Standard neuropsychological tests of memory typically only test at delays of up to 30-minutes. Given that in ALF information is thought to be lost over longer time periods than 30-minutes, some patients' memory impairment may go undetected. In the absence of standardised tests it has been necessary for researchers to create their own materials and develop innovative procedures to assess forgetting over extended delays. Developing methodologically sound assessments of ALF is important clinically to ensure accurate assessment and inform evidence-based clinical recommendations and interventions. In time, it is hoped that research into ALF will lead on to the development of standardised tests which can be used for this purpose.

To understand novel patterns of forgetting, it is important to consider theoretical literature on the underlying processes of consolidation. 'Consolidation' refers to the hypothetical processes that stabilise a memory trace within long-term storage so that it can be stored and retrieved later i.e. making it less resistant to forgetting. Whilst consolidation may continue for weeks, months or even years (Squire & Alvarez, 1995) it is generally assumed that its efficacy can be evaluated after relatively short delays, hence why standardised assessments of memory typically test after 30-minutes. There are two main theories of consolidation; The Standard Model (Squire, 1992; Squire, Cohen & Nadel, 1984) and the Multiple Trace Theory (Nadel & Moscovitch, 1997). The Standard Model assumes that a short-term consolidation process within the hippocampus and related structures in the medial temporal lobes bind information into a memory trace within seconds and then long-term consolidation processes establish a permanent memory trace within the neocortex. The Multiple Trace Theory proposes a

role of the hippocampus in an extended period of consolidation whereby every reactivation of a memory produces a new trace within the medial temporal lobe rather than neocortical regions, thus implicating a longer term role for the medial temporal lobes in memory stabilisation. Forgetting is observed when underlying processes of consolidation are compromised and information is not established in memory.

It has been hypothesised that seizure activity and/or structural damage may disrupt extended consolidation processes, although the link between ALF and TLE remains to be confirmed as recent reviews (Bell & Giovagnoli, 2007; Butler & Zeman 2008) have highlighted mixed results. Some studies have found ALF in TLE patients (Martin et al., 1991; Blake et al., 2000; Manes et al., 2005; Mameniskiene et al., 2006; Butler et al., 2007); however others have not (Giovagnoli et al., 1995; Bell et al., 2005; Bell, 2006). This lack of consensus may be due to methodological differences and the fact that this area of study is fraught with methodological difficulties. Given that existing studies may be limited by methodological confounds, it is essential that researchers take these difficulties into account when designing future research studies.

Although ALF is a specific form of forgetting, the methodological problems which can be encountered are associated with investigating all kinds of forgetting. In any forgetting study, the aim is usually to compare forgetting rates between groups over time and therefore the fundamental methodological principles are the same. In considering the issues applicable to investigating ALF, it is therefore relevant to consider the wider literature on forgetting. As Isaac and Mayes (1999a) acknowledged, there are a number of potentially serious methodological problems which can arise when attempting to compare the forgetting rates of amnesic and healthy participants.

This review aims to evaluate methodological problems within forgetting research in general and ALF in particular. Revisiting this literature is timely in a climate when many researchers are developing new assessments and procedures to study ALF. In Part I, the literature addressing methodological issues in the assessment of forgetting rates is summarised. This review will not reiterate the complex theoretical and mathematical debates around the assessment of forgetting rates, rather it attempts to summarise different opinions and provide a reference point for the issues to consider when embarking on research into ALF. In Part II, existing case reports and group studies of ALF will be reviewed with emphasis on experimental design to evaluate the extent to which key methodological issues have been addressed.

SEARCH STRATEGY

A thorough search of psychological and medical literature was performed. The initial search strategy is summarised in Table 1 (searches resulting in zero matches are not shown). Broad search terms were used for Part I as specific methodological terms did not identify any relevant articles. Searches were limited to peer-reviewed, human studies for which the full text was available in English.

Following initial searches, titles and available abstracts were examined for relevance and reference lists were trawled to identify reports which were not indexed. Trawling references proved to be the source of many articles identified for Part I due to their publication dates preceding indexing. Only papers considering methodological factors which could be controlled for within experimental designs were included. This process resulted in a total of 22 articles being identified as relevant to Part I and 19 articles relevant to Part II.

Table 1. Summary of initial search

	Search Terms	Database	Matches
Part I	"Forgetting rates" OR "rate of forgetting" OR "accelerated long-term forgetting" OR "long-term amnesia" OR "long-term forgetting"	PsychINFO	167
		MEDLINE	122
		Web of Knowledge	1476
	"overlearning" AND "forgetting"	PsychINFO	2
Part II	"Accelerated long-term forgetting" AND "epilepsy"	PsychINFO	5
		MEDLINE	4
		Web of Knowledge	13
	"Long-term amnesia" AND "epilepsy"	PsychINFO	3
		MEDLINE	4
		Web of Knowledge	6

PART I: Methodological Issues in Assessing Forgetting Rates

The key methodological issues relating to the comparison of forgetting rates were identified to be selection of appropriate control participants, choice of test material and procedures and the interaction between degree of initial learning and rate of forgetting.

Selection of Control Participants

In the absence of appropriate standardised tests, researchers must employ a control group. It is widely accepted that patient and control groups should be as similar as possible however the variables considered important have been the focus of debate. As Mayes (1986) stressed, assessments of memory should include measurement of intelligence as in healthy people IQ and memory are positively correlated. It is also well documented that an age-related decline in memory exists and therefore it is important the groups being compared are of a similar age. With specific regard to forgetting over long-delays, MacDonald, Stigsdotter-Nelly, Derwinger, and Backman (2006) taught 136 participants 4-digit numbers to perfection and tested their retention after 30-minutes, 24 hours, 7 weeks and 8 months. Their results demonstrated that older age and poorer cognitive performance (on measures of episodic memory, perceptual speed and working memory) predicted accelerated forgetting, particularly within the first 24 hours. The clear conclusion is that control and patient groups should be matched for age and IQ to avoid confounding variables.

Test Materials & Procedures

Five issues relating to test materials and procedures were identified. Each is discussed with particular consideration given to the relevance for studies of ALF.

Material Specificity

Forgetting can be assessed by visual material, typically pictures or verbal material such as stories and word lists. Hart and O'Shanick (1993) recommended that sole reliance on visual stimuli limits the generalisability of findings. By assessing forgetting rates for different types of material one can better determine whether rapid forgetting reflects a

general memory consolidation deficiency or deficits in information processing for particular types of information.

Butler and Zeman (2008) found existing data to be inconclusive regarding whether laterality of seizure focus leads to material-specific forms of ALF. Therefore, both verbal and visual material should be routinely included when studying ALF.

Assessment Procedure

Memory studies typically use free recall or recognition procedures to assess forgetting. In free recall paradigms participants are asked to recollect the information they have learnt, in any order, without cues. Recognition tests require participants to correctly remember something they have previously encountered when it is presented again. Mayes (1986) stressed the importance of including both procedures in order to be able to examine the nature of retrieval deficits in more detail. In relation to amnesia, Isaac and Mayes (1999a) noted that many previous studies of forgetting rates focused only on recognition memory. Given evidence that recognition and recall memory may be affected differently in amnesia, they argued for the importance of examining both. There is some evidence to suggest that ALF affects both recall and recognition, but the findings are inconsistent (Butler & Zeman, 2008). Therefore, until conclusive evidence is available, it seems important to examine both recall and recognition when studying ALF.

Even within a recognition paradigm, differences in test procedure may be important. For example, Freed and Corkin (1988) compared the performance of patient H.M. on a forced choice recognition procedure (where subjects view two slides simultaneously and are asked to judge which one they have seen before), a yes-no recognition procedure

(where subjects view a single slide and are asked to judge whether or not they have seen the slide before), and a yes-no(new) procedure (where subjects judge whether or not the slide is new, thus focusing on aspects of novelty). They found that the different recognition procedures yielded discrepant results and argued for the superiority of the forced-choice procedure as this induced the least variability. The reason why this was the case was unclear so to ensure reliable assessment of recognition over long delays it would be sensible to pilot test material first.

Floor and Ceiling Effects

Ceiling effects arise when a test is not challenging enough for high functioning individuals who therefore achieve the maximum score. In contrast, floor effects arise due to task difficulty causing performance to be at the lowest point. Ceiling and floor effects are problematic because there is no scope to measure improvement (ceiling effect) or decline (floor effect) and so the true group mean cannot be ascertained. Consequently, the measured statistical variance will be below its true level and therefore the sensitivity of experiments designed to determine if the average of one group is significantly different from another will be reduced. Questions have arisen about whether it is preferable to avoid analysing data that appears to be approaching the floor (e.g. Slamecka & McElree, 1983) or presume that forgetting may still be occurring (even though it is not detectable by the dependant measure) and include the data.

This issue is particularly pertinent since as Isaac and Mayes (1999a) highlight, amnesic participants are likely to perform at floor levels and control participants at ceiling levels. In the study of ALF, ceiling effects at short delays may lead to forgetting rates in healthy controls being underestimated. Therefore, in designing tests to assess ALF systematic piloting should be undertaken to ensure that healthy participants are not

performing at ceiling levels at short delays nor at floor levels at long delays. This may involve manipulating interval lengths between testing sessions. For example, if floor effects are observed, the delay could be shortened and if ceiling effects are observed, the delay could be increased.

Rehearsal Effects

Rehearsal is the act of repeatedly practising information to be remembered. Evidence consistently suggests that rehearsal is beneficial in consolidating memories. Since rehearsal effects have not been systematically examined with respect to ALF, to avoid confounding results, the potential for rehearsal during delays should be eliminated where possible (Butler & Zeman, 2008). Not forewarning participants about later requests for recall is one means of avoiding this issue. However, if participants are aware of the nature of the study or if it is a repeat assessment within clinic, they are likely to predict that they will be asked about the information again. Another option is to purposefully select stimuli which are difficult to rehearse. This may include a large number of discrete visual designs rather than a semantically related story (Butler & Zeman, 2008).

A related issue is the potential effects of repeated recall. Jansari, Davis, McGibbin, Firminger, and Kapur (in press) assessed the effect of frequent recall on subsequent memory performance in a participant with TLE. The participant had to recall two stories at all five time points (30-minutes, 1 day, 1 week, 2 weeks, 4 weeks), and recall a further 8 stories at a single time point. Free recall and recognition data were compared across stories and the results suggested that repeated recall had a protective effect on forgetting, without which story recall fell to floor levels within two weeks. This study illustrates that repeated recall (without re-representation) may help

counteract the effects of ALF. To avoid this confounding effect, different stimuli could be tested at each time point.

Delay Period

Isaac and Mayes (1999a) pointed out that studies which matched performance between groups at an immediate delay may be confounded by the risk that performance is partially based on short-term memory (STM). Short-term memory refers to the capacity to hold a limited amount of information in mind for a period of seconds. In memory impaired populations, STM is usually normal; it is long-term memory (LTM) which is impaired. This combination may result in the appearance of fast forgetting as impairments observed at longer delays may reflect a lack of contribution from normal STM processes rather than a deficit in LTM. This is an important distinction because, as Trahan and Larrabee (1993) emphasised, one must be certain that information has been successfully stored in LTM; otherwise failure to retrieve it later may represent a disruption in the transfer process between STM to LTM as oppose to forgetting. With this in mind, Isaac and Mayes (1999a, 1999b) included a 15-second distracter task prior to immediate recall and evidenced that this ensured recall was not reliant on STM processes.

With regard to investigating ALF, best practise would therefore be to test subjects following a filled delay of at least 15 seconds. This will allow for accurate measurements of initial learning and consolidation, thus providing a valid assessment of forgetting from LTM. The inclusion of another test after approximately 30-minutes will then allow for analysis of the forgetting curve. This procedure will provide evidence that impairments observed at longer delays signify true ALF rather than memory impairment of the amnesic-type which would be picked up at shorter delays.

To summarise, in developing assessments to study ALF, a combination of verbal and visual material should be used, incorporating tests of recall and recognition. Stimuli should be piloted carefully to establish the type of material and paradigms which induce least variability, have a low risk of floor and ceiling effects and a limited potential for rehearsal. Of further note, procedures should also ensure that immediate recall is based on LTM processes alone.

Degree of initial learning and rate of forgetting

There is considerable debate in the literature regarding comparing forgetting rates of groups who may be performing at very different levels. There are two main hypotheses to consider. The first maintains that degree of initial learning does not influence subsequent rates of forgetting (Slamecka & McElree, 1983; Slamecka, 1985) whilst the second argues that forgetting rates cannot be compared unless initial learning is equated (Loftus 1985a, 1985b).

Slamecka and McElree's (1983) argument for the first hypothesis was based on three experiments involving categorized word lists, paired associate lists and sentence lists respectively. In each experiment learning was varied and retention tested at three intervals (immediate, 1 day, 5 days). Learning was adjusted by altering the number of study trials (one trial: low degree of learning or three trials: high degree of learning). Un-cued recall and cued recall was measured and compared between groups. The consistent finding across all experiments was that the number of study trials affects the intercept but not slope (i.e. the rate) of forgetting. This led to the conclusion that variations in degree of learning are independent of the subsequent course of normal forgetting and consequently it was argued that equating initial acquisition is not necessary. The standard method of comparing forgetting rates by examining whether

there is an interaction between forgetting rate and retention interval between conditions was therefore favoured. Bogartz (1990a, 1990b) agreed with the assertion that forgetting rate is independent of original learning but rejected Slamecka & McElree's approach in favour of a 'psychological approach' to evaluating forgetting curves.

Loftus (1985a, 1985b) and Loftus and Bamber (1990) disputed the claim that degree of initial learning has no impact on later forgetting and argued that the traditional test of interaction encompasses an inherent scaling problem which can lead to the conclusion that forgetting rates are equal when they are not. To circumvent this problem, Loftus proposed an alternative method which involves comparing the horizontal distance between forgetting curves over time. After analyzing data using this method, Loftus concluded that a higher degree of original learning leads to a slower rate of forgetting reinforcing the belief that initial learning between groups must be equated. Paul (1994) agreed with the assumption that interpretable forgetting comparisons can only be made if the effects of initial learning are eliminated and offered an alternative "shape method" of making forgetting comparisons.

Whilst a definitive conclusion is not possible to formulate, an awareness of the debates will assist researchers in making sound methodological decisions. As Wixted (1990) pointed out, the primary objectives of the researcher are likely to determine the most appropriate method. Despite this, most researchers have continued to use the standard test of interaction without any apparent consideration of the methodological issues (Paul, 1994). Although choosing this method seems reasonable as the added complexity provided by mathematical models is unlikely to be required to test the hypotheses of clinically relevant research into ALF, potential scaling problems must be

still considered. Ways in which scaling problems can be dealt with are discussed in the next section.

Matching Initial Learning

It has been argued that scaling problems can be eliminated by matching initial learning (Huppert & Piercy, 1978). Shuell and Keppel (1970) outlined several matching procedures, namely administering differential numbers of exposure trials, using different length stimulus lists or employing study intervals of different durations. Shuell and Keppel duly noted that although such procedures may successfully equate performance, little is known about the consequences of doing so on forgetting. Potential matching procedures will now be considered in more detail.

Extended Exposure Times

Shuell and Keppel (1970) chose to equate learning of word lists using different presentation rates (1 or 5 seconds). Prior to this, participants had to complete a pre-test which involved remembering a list of words. They were then ranked on the basis of how many words they recalled and categorised as slow or fast learners accordingly. To equate learning, slow learners received the longer presentation rate. When retention was tested after 24 and 48 hours, results demonstrated that differences in retention were minimal when degree of original learning is equated.

Huppert and Piercy (1978) were the first to use a matching procedure with memory impaired populations. They introduced the method of allowing amnesic participants longer exposure times to the target material during presentation; a procedure which has been used extensively in forgetting studies to date. In their study, the performances of two groups (7 amnesic participants and 6 controls) were matched on a picture

recognition task after a 10-minute interval. To equate initial learning, amnesic participants were permitted 4 or 8 seconds to view each picture as opposed to controls who were only allowed 1 second. Memory was tested again after 1 day and 7 days using a yes-no recognition procedure. Analysis revealed that recognition performance declined over time in both groups, but the rate of decline did not differ between groups. The authors interpreted this to reflect an initial learning deficit amongst amnesic patients (which was rectified by increased exposure time at presentation).

Isaac and Mayes (1999a) argued that Huppert and Piercy's method biases against finding that amnesic participants forget faster. The rationale for this critique is that amnesic participants receive longer exposure to the test stimuli and so, because the delay is timed from the end of the presentation phase, the mean item to test delay period is longer than it is for controls. Consequently, forgetting rates of the amnesic group could be underestimated on the assumption that older memories decline at a slower rate (Mayes, 1986). On this basis, Mayes (1986) argued for the importance of matching the average item-test delay by working out the necessary exposure time for the most impaired participant and then ensuring all participants have the same delay between item presentations.

Multiple Presentation Procedure

Isaac and Mayes (1999a) utilized a multiple presentation procedure as an alternative to the extended exposure method. Instead of a single extended presentation time for each item, multiple presentations were given. This method ensured the final multiple presentation of an item for the amnesic group occurred at the same time as the single presentation of an item for the control group.

Teaching to Criterion

Teaching to criterion involves repeatedly presenting material until a learning criterion (e.g. 100% accuracy on two successive trials) is reached. Butler and Zeman (2008) make the point that this method of matching learning poses the risk of the material being over-learnt; leading to the possibility that early forgetting is masked by ceiling effects. Overlearning is commonly defined as further study of material which has already been learnt to a criterion of one perfect trial. Given that criterion levels are almost always set at a level which exceeds accuracy on one trial, overlearning is indeed a risk inherent to this approach.

Butler and Zeman's argument for the negative effects of overlearning is based on the assumption that repeated learning trials lead to a performance improvement over shorter delays followed by the finding that memory is impaired at longer delays. Therefore, if this method is used in studies of ALF, one must be cautious in interpreting forgetting observed at longer delays as this may reflect initial overlearning having led to the underestimation of forgetting at the shorter delay.

A viable alternative may be the selective reminding procedure (Buschke, 1973; Buschke & Fuld, 1974) whereby only non-remembered items are presented again at further learning trials. However, this method also dictates that participants must recall the item on two consecutive learning trials. Given the aforementioned definition of overlearning, this arguably gives rise to the same issue. Limiting further learning trials to items which have not been recalled at all may more adequately avoid overlearning and subsequent confounds.

In summary, matching initial learning between groups is important, particularly if traditional tests of interaction are used to compare forgetting rates and scaling problems need to be considered. A number of ways to equate initial learning having been identified and there is some suggestion that the multiple presentation procedure may be the superior method. Regardless of the chosen procedure, researchers should be mindful of the potential implications in the interpretation of their results.

PART 1: SUMMARY AND RECOMMENDATIONS

This review has identified the following key methodological considerations which researchers should take into account when designing experiments to investigate ALF:

1. Patient and control groups should be matched, at least for age and intellectual ability.
2. Ideally, both verbal and visual test material should be used.
3. Ideally, forgetting should be measured using both recall and recognition tests.
4. Ceiling and floor effects should be avoided as far as possible.
5. The potential for rehearsal and repeated recall should be avoided as far as possible.
6. The immediate delay period should be long enough to ensure information is stored in LTM and retrieval is not reliant on STM processes
7. Effort should be made to equate initial learning (whilst avoiding over-learning).

PART II: Do recent studies of ALF in epilepsy meet the recommendations?

Nineteen studies investigating ALF in epilepsy have been identified. Many of the studies included have already been reviewed in recent papers (Bell & Giovagnoli, 2007; Butler & Zeman, 2008). However, as previously discussed the specific focus here is to review their methodology and evaluate the extent to which key methodological issues have been considered.

Overview of Case Reports

Eight case reports of ALF in epilepsy were identified (Cronel-Ohayon et al., 2006; Holdstock, Mayes, Isaac, Gong & Roberts, 2002; Jansari et al., in press; Kapur et al., 1997; Kapur et al., 1996; Lucchelli & Spinnler, 1998; Mayes et al., 2003; O'Connor, Seiggreen, Ahern, Schomer, & Mesulam, 1997). Two of these publications report data on the same patient, JL (Holdstock et al., 2002; Mayes et al, 2003). All cases studies were adults with the exception of Cronel-Ohayon et al. (2006). Demographic data of participants and the main findings of case studies can be viewed in Table 2.

In many case studies, the participant had a history of temporal lobe epilepsy (TLE) amidst complex aetiologies, namely closed head injury (Holdstock et al., 2002; Kapur et al., 1996; Mayes et al., 2003), paraneoplastic limbic encephalitis and high seizure frequency (O'Connor et al., 1997), and late onset seizures with no clear cause (Jansari et al., in press; Kapur et al., 1997; Lucchelli & Spinnler, 1998). Structural brain imaging was abnormal in all cases with the exception of two patients (Jansari et al., in press; Lucchelli & Spinnler, 1998). Damage was limited to the temporal lobes in all but the case presented by Holdstock et al. (2002) and Mayes et al. (2003).

Table 2: Demographic details and main findings in case studies of ALF

Authors (year)	**ALF evidence?** (delay 1st seen)	**Sample Size**		**Mean Age** (SD)		**Sex**		**IQ** (SD)		**Brain Pathology**	**Seizure Lateralization**
		Patient	*Controls*	*Patient*	*Controls*	*Patient*	*Controls*	*Patient*	*Controls*	*Patient*	*Patient*
Cronel-Ohayon et al.(2007)	Yes (7 days)	1(JE)	1	18	18	M	M	90	i/n/p	L-AMG	L
Holdstock et al. (2002)	Yes (3 weeks)	1(JL)	10	40	41.1 (3.03)	F	F	122	113.5 (8.2)	Bi-TL HC normal	R
Jansari et al. (in press) Experiment 1	Yes (1 day)	1(RY)	8	63	66.3 (4.9)	M	3M-5F	118	117.9 (6.29)	None	R
Experiment 2	Yes (1 day)	1(RY)	6	63	61.8 (5.41)	M	M	118	122 (5.79)		R
Kapur et al. (1996)	Yes (6 weeks)	1(SP)	3	50	46.3	F	F	94	i/n/p	Left-TL	i/n/p
Kapur et al. (1997)	Yes (40 days)	1(PA)	4	62	65.3	F	F	124	121.1	Left-HC	L
Lucchelli & Spinnler (1998)	Yes (7 days)	1(GB)	2	65	63.5	M	i/n/p	120	i/n/p	Mild ventricular asymmetry L>R	L
Mayes et al. (2003)	Yes (3 weeks)	1(JL)	10	41	40.6 (2.7)	F	i/n/p	122	116 (10.9)	Bi-TL HC normal	R
O'Connor et al. (1997)	Yes (24 hours)	1(JT)	1	42	40	M	M	127	i/n/p	Bi-MTL	Bi

M=male, F=female, i/n/p = information not presented, R=right, L=left, Bi=bilateral, TL=temporal lobe, MTL=mesial temporal lobe, HC=hippocampus, AMG=amygdala

Overview of Group Studies

Ten group studies of ALF in adults were identified (Bell, 2006; Bell, Fine, Dow, Seidenberg & Hermann, 2005; Blake, Wroe, Breen, & McCarthy, 2000; Butler et al., 2009; Butler et al., 2007; Giovagnoli, Casazza, & Avanzini, 1995; Helmstaedter, Hauff, & Elger, 1998; Mameniskiene, Jatuzis, Kaubrys, & Budrys, 2006; Manes, Graham, Zeman, de Lujan Calcagno, & Hodges, 2005; Martin et al., 1991) and one study examining ALF in children with idiopathic generalized epilepsy (Davidson, Dorris, O'Regan, & Zuberi, 2007). Demographic data of participants and the main findings of group studies can be viewed in Table 3.

The majority of adult studies sampled TLE patients. Three studies (Butler et al., 2009, Butler et al., 2007; Manes et al., 2005) report data on patients with Transient Epileptic Amnesia (TEA), a specific subgroup of TLE and one which is thought to have a particularly intimate relationship with memory (Butler et al., 2009). The use of different subgroups of epilepsy patients immediately reduces the comparability of these studies.

All studies identified will now be reviewed for their adherence to the methodological considerations established in Part I. For a summary of whether each study was evaluated to have met the recommendations, see Tables 4 and 5 for case studies and group reports respectively.

Table 3: Demographic details and main findings in group studies of ALF

Authors (year)	ALF evidence? (delay)	Sample Size		Mean Age (SD)		Sex		IQ (SD)		Brain Pathology	Seizure Lateralization
		Patients	*Controls*	*Patients*	*Controls*	*Patients*	*Controls*	*Patients*	*Control*	*Patients*	*Patients*
Bell et al.(2005)	No (24 hours)	42	49	37 (11.4)	37 (11.8)	14M 28F	22M 27F	93.5 (14.2)	104 (12.7)	None	20R 22L
Bell (2006)	No (2 weeks)	25	25	39 (10)	35 (11)	10M 15F	8M 17F	94 (12)	104 (10)	None 6 postop	6R, 11L, 2 Bi 24% uncertain
Blake et al. (2000)	Yes (8 weeks)	21(14 TLE)	16	33.76 (9.72)	46.25 (14.54)	7M 14F	6M 10F	103.65 (12.72)	101.88 (13.20)	HS 5/14 TLE group	10R 11L
Butler at el. (2007)	Yes (1 week)	24	24	67 (8.7)	67.7 (8.2)	14M 10F	10M 14F	124.3 (10.4)	120 (14.4)	None	i/n/p
Butler et al. (2009)	Yes (1 week)	22	20	66.4 (8.8)	67.5 (8.6)	12M 10F	8M 12F	124.7 (10.7)	121.2 (14.9)	<HC volume	i/n/p
Davidson et al. (2007)	Yes (1 week)	21	21	11.5	11.9	7M 14F	>F	99.4 (14.4)	98.5 (11.6)	i/n/p	i/n/p
Giovagnoli et al. (1995)	No (13 days)	24	25	38 (11.82)	37.5 (10.88)	14M 14F	13M 12F	i/n/p	i/n/p	None	12R 16L
Helmstaedter et al. (1998)	Yes (1 week)	55	21	26.9	29.4	27M 28F	11M 10F	100 (11)	110 (12)	10 none, 14 HS, 16 tumors, 4 hetertopia, 11 other TL	27R 28L
Martin et al.(1991)	Yes (24 hours)	21	21	31 (7.5)	40 (11.4)	10M 11F	6M 15F	91.4 (9.9)	101 (10.1)	6 postop	8R 13L
Mameniskiene et al. (2006)	Yes (4 weeks)	70	59	33 (9.5)	31 (9.5)	29M 41F	19M 40F	i/n/p	i/n/p	11 TL lesion	i/n/p
Manes et al.(2005)	Yes (6 weeks)	7	7	57 (8.1)	64	6M 1F	i/n/p	115.3 (8.5)	110.5 (6.7)	None	i/n/p

Studies reporting separate statistics for right and left TLE patients have been combined in this summary. M=male, F=female, i/n/p = information not presented, R=right, L=left, Bi=bilateral, TL=temporal lobe, HC=hippocampus, HS=hippocampal sclerosis, postop=undergone epilepsy surgery

Table 4. Case reports of ALF in epilepsy: Methodology Evaluation

Authors (year)	Matched Controls?	Test Material	Recall & Recognition?	Ceiling & floor effects avoided?	Rehearsal avoided?	Immediate delay after 15 seconds?	Matching procedure?	Initial learning equated?
Cronel-Ohayon et al.(2006)	Age-yes IQ-no	Verbal Visual	No	Yes	No	No	No	Yes
Holdstock at al.(2002)	Age-yes IQ-yes	Verbal	No	No	Yes	Yes	Yes	Yes
Jansari et al.(in press)	Age-yes IQ-yes	Verbal	Yes	No	Yes	No	No	Yes
Kapur at al. (1996)	Age-yes IQ-no	Verbal Visual	Yes	No	No	No	No	Yes
Kapur et al. (1997)	Age-yes IQ-yes	Verbal Visual	Yes	No	No	No	No	Yes
Lucchelli & Spinnler (1998)	Age-yes IQ-no	Verbal Visual	No	No	No	No	No	Yes
Mayes et al. (2003)	Age-yes IQ-yes	Verbal Visual	Yes	No	Yes	Yes	Yes	Yes
O'Connor et al. (1997)	Age-yes IQ-no	Verbal	No	No	No	No	Yes	Yes

Table 5. Group studies of ALF in epilepsy: Methodology Evaluation

Authors (year)	Matched Controls?	Test Material	Recall & Recognition?	Ceiling & floor effects avoided?	Rehearsal avoided?	Immediate delay after 15 seconds?	Matching procedure included?	Initial learning equated?
Bell et al.(2005)	Age-yes IQ-no	Verbal Visual	No	Yes	Yes	No	Yes	No
Bell (2006)	Age-yes IQ-no	Verbal	Yes	Yes	Yes	No	No	No
Blake et al.(2000)	Age-yes IQ-yes	Verbal	Yes	No	Yes	No	Yes	Yes
Butler et al.(2007)	Age-yes IQ-no	Verbal Visual	Yes	No	Yes	No	Yes	Yes
Butler et al.(2009)	Age-yes IQ-no	Verbal Visual	No	Yes	No	No	Yes	Yes
Davidson et al. (2007)	Age-yes IQ-yes	Verbal Visual	Yes	Yes	Yes	No	Yes	No
Giovagnoli et al. (1995)	Age-yes IQ-no	Visual	No	Yes	No	No	Yes	No
Helmstaedter et al. (1998)	Age-yes IQ-no	Verbal Visual	No	Yes	Yes	No	No	No
Martin et al. (1991)	Age-no IQ-no	Verbal	No	Yes	Yes	No	Yes	Yes
Mameniskiene et al.(2006)	Age-yes IQ-no	Verbal Visual	No	Yes	No	No	No	No
Manes et al.(2005)	Age-yes IQ-yes	Verbal Visual	Yes	No	No	No	No	Yes

Selection of Control Participants

The recommendation from Part I was that patient and control groups should be matched for age and intellectual ability. All studies with the exception of Martin et al. (1991) successfully matched patients and controls for age. Regarding matching groups for intellectual ability, there is a discrepancy in the way this is achieved. The three methods utilized are pre-morbid IQ as measured by the National Adult Reading Test (NART) or Wechsler Test of Adult Reading (WTAR), number of years in education or current intellectual functioning as measured by Wechsler Adult Intelligence Scale. It is argued here that with neurologically impaired groups it is important that current ability is the basis for matching. Matching by pre-morbid ability (as predicted by a reading-derived score or number of years in education) is not adequate as there may have been a decline from previous ability.

Based on these criteria, in eight group studies (Bell, 2006; Bell et al., 2005; Butler et al., 2009; Butler et al., 2009; Giovagnoli et al., 1995; Helmstaedter et al., 1998; Mameniskiene et al., 2006; Martin et al., 1991) IQ was not adequately matched. To account for differences in intellectual ability, Helmstaedter et al. (1998) and Martin et al. (1991) computed an analysis of covariance (ANCOVA), taking IQ as a covariate. However, as Adams, Brown and Grant (1985) argue this is an unsatisfactory resolution. With respect to case studies, only four report matching participants on the basis of current IQ (Holdstock et al., 2002; Jansari et al., in press; Kapur et al., 1997; Mayes et al., 2003).

Test Materials & Procedures

This review has found that the materials used in existing studies vary considerably. Some studies have utilised standardised tests and added a longer delay whereas others

have designed new material. The most commonly adapted existing tests are the Wechlser Memory Scales-Revised (Bell, 2006; Kapur et al., 1997; Kapur et al., 1996; Manes et al., 2005), Rey Auditory Verbal Learning Test (Butler et al., 2009; Butler et al., 2007; Cronel O'Hayon et al., 2007; Helmstaedter et al., 1998; Mameniskiene et al., 2006 ;) and Rey-Osterreith Complex Figure (Cronel O'Hayon et al., 2007; Lucchelli & Spinnler, 1998; Mameniskiene et al., 2006; Mayes et al., 2003).

Helmstaedter et al. (1998) devised an ecologically valid assessment of ALF which was termed a 'Memory in Reality Test'. The situation to be remembered was the standard neuropsychological examination all participants experienced. Although within the study this procedure successfully combined daily memory for individually experienced events with objective testing, the limitation lies in the unfeasibility of replication and standardisation for use in clinical practise.

Ideally, more refined tests would be developed specifically for the assessment of ALF. In doing so, further investigation of the types of tests which are sensitive to and provide an ecologically valid assessment of ALF is warranted.

Material Specificity and Assessment Procedures

The conclusions drawn in Part I indicated that studies should employ both verbal and visual test material and evaluate forgetting using a combination of recall and recognition paradigms. This review has identified that many studies of ALF have not met this desired standard.

Of the eight case reports identified, five employed verbal and visual test material (Cronel-Ohayon et al., 2007; Kapur et al., 1997; Kapur et al., 1996; Lucchelli &

Spinnler, 1998; Mayes et al., 2003), only three of which assessed recall and recognition in both modalities (Kapur et al., 1997; Kapur et al., 1996; Mayes et al., 2003). Of the eleven group studies, seven employed verbal and visual material (Bell et al., 2005; Butler et al., 2009; Butler et al., 2007; Davidson et al, 2007; Helmstaedter et al., 1998; Mameniskiene et al., 2006; Manes et al., 2005). Of these, only two (Davidson et al., 2007; Manes et al., 2005) assessed recall and recognition in both modalities. Studies failing to include verbal and visual material are limited by their inability to claim strong evidence for material specificity. For example, in absence of visual tasks, Blake et al. (2000) could not offer an explanation for subjective reports of memory difficulties in patients with right TLE who performed adequately on verbal tasks.

Floor and Ceiling Effects

The recommendation from Part I was that floor and ceiling effects should be avoided as far as possible. It is not clear from the information published to what extent most studies endeavoured to do this. Floor effects or ceiling effects arose to some extent in all case studies with the exception of Cronel-Ohayon et al. (2007). A common problem is that the performance of patients at long delays is frequently at floor level (at least for some tests). Holdstock et al. (2002) made a concerted effort to ensure tests were sensitive by avoiding floor effects on an item by item basis. However, their experimental manipulations were not successful as a ceiling effect occurred at 24 hours. Holdstock et al. acknowledge that this may have concealed forgetting between 24 hours and 3 weeks.

Floor effects were also problematic in group studies by Blake et al. (2000) and Manes et al. (2005). In Blake et al.'s study, five of the left-temporal group and one right-temporal patient scored at floor on story recall after eight weeks. Manes et al. found

that four patients scored zero on story recall at 6 weeks. In addition, design recall data had to be eliminated due to all patients and many controls performing at floor levels.

It is clear from this review that future studies need to do more to avoid floor and ceiling effects through careful piloting of their test material. The indication is that manipulating the length of the long delay, testing at multiple long delay points and varying task difficulty across delays may be effective.

Rehearsal Effects

The conclusion from Part I was that the potential for rehearsal should be avoided where possible, however many publications do not comment on whether this issue was considered. Where rehearsal is actively discouraged, the predominant method is to avoid telling participants that their memory will be re-tested (Bell, 2006; Bell et al., 2005; Helmstaedter et al., 1998; Holdstock et al., 2002; Martin et al., 1991; Mayes et al., 2003). However, if the ultimate goal is to develop repeatable tests for clinical practise, participants will have to be told that their memory will be examined again in order to avoid creating future confounding variables. An arguably weak alternative is to explicitly request participants not to rehearse the material, an approach adopted by Blake et al. (2000), Butler et al. (2007) and Davidson et al. (2007).

A further issue is the inappropriateness of recruiting friends and family for control groups (Bell, 2006; Bell et al., 2005; Blake et al., 2000). Given the likelihood that most people would be tempted to discuss the process, the probability of rehearsal is increased. If there is no alternative, as Blake et al. and Butler et al. (2007) ensured, care should be taken to ensure that family members are presented with different material.

Delay Period

The importance of ensuring that information is stored in LTM prior to an immediate delay test has been argued in Part I. The recommendation is that there should be a filled delay of at least 15 seconds to eliminate the risk that retrieval is reliant on STM processes. With the exception of Holdstock et al. (2002) and Mayes et al. (2003) who utilised a 20-second immediate filled delay, no studies explicitly mention having considered this. Of note, studies which modified existing tests followed standard administration procedures which would not have accommodated a filled delay before immediate recall. All studies however did include a 30-minute delay which is critical to claiming reliable evidence of ALF.

Matching Initial Learning

No consensus has been reached regarding whether or not degree of initial learning affects rate of forgetting. This raises issues for interpretation in those studies which chose to accept different acquisition levels and compare the overall shape of forgetting curves over time (Bell et al., 2005; Bell, 2006; Mameniskiene et al., 2006). The conclusion from Part I is that matching initial learning is important to avoid scaling problems inherent in standard tests of interaction.

All case study patients achieved comparable immediate recall to controls with the exception of story recall in the case presented by Lucchelli and Spinnler (1998). Largely, this occurred without manipulating presentations, however O'Connor et al. (1997) taught participants to criterion and Holdstock et al. (2002) allowed participants greater exposure to the items which would be tested after longer delays. Seven group studies (Bell et al., 2005; Blake et al., 2000; Butler et al., 2007; Butler et al., 2009; Davidson et al., 2007; Giovagnoli et al., 1995; Martin et al., 1991) manipulated

experimental procedures in an effort to match initial learning. In five cases this seems to have been successful, however when performance is at ceiling on immediate or short delay trials (e.g. Blake et al., 2000; Butler et al., 2007), it is difficult to make a definitive judgement that learning was successfully equated. A limitation of studies where initial learning was not matched (Bell, 2006; Bell et al., 2005; Mameniskiene et al., 2006) is that subsequent forgetting rates may have been underestimated in the patient group.

Of those studies which attempted to equate initial learning, five taught participants to criterion (Blake et al., 2000; Butler et al., 2007; Davidson et al., 2007; Martin et al., 1991; O'Connor et al., 1997), however the potential limitations associated with overlearning were not overtly considered. Three studies (Bell et al., 2005; Giovagnoli et al., 1995; Martin et al., 1991) employed the selective reminding technique (Buschke, 1973; Buschke & Fuld, 1974) which in part circumvents the issue of overlearning. None of the studies applied the multiple presentation procedure which was highlighted to be a particularly viable method in Part I.

SUMMARY AND CONCLUSIONS

This review identified seven methodological issues which are important to take into account when investigating ALF. More specifically, it is recommended that groups are matched for age and intellectual ability, both verbal and visual tests are used in combination with recall and recognition paradigms and the immediate delay is long enough to ensure information has been stored in LTM. In addition, experimental manipulations should be made to equate initial learning, avoid ceiling and floor effects and minimise opportunities for rehearsal of test material.

Existing studies investigating ALF in epilepsy were then evaluated to determine whether pertinent methodological issues were considered. On this basis, Mayes et al. (2003) is proposed to be the most methodologically sound case study having been judged to have complied with all but one of the recommendations. Furthermore, although the patient's verbal recall was at floor at the long delay, reliable evidence of ALF could still be concluded as recall of the story was within normal limits at 20-seconds and 30-minutes yet after 3 weeks the patient was completely unable to remember the learning episode. Perhaps a shorter long-delay of one week would have evidenced ALF and kept performance off the floor. Based on the information reported, the case report by O'Connor et al. (1997) only met the recommendation to match initial learning. In this study, the patients' brother was the control participant and although they were considered to have similar educational backgrounds, no formal measures of IQ were taken. Furthermore, only verbal recall was assessed so no evidence for a material specific deficit could be claimed. Nevertheless, as one of the earliest studies of this unusual pattern of forgetting, O'Connor et al. raised pertinent theoretical questions for further investigation.

A significant limitation within group studies has been the difficulty matching groups for IQ. Unfortunately this is likely to remain a challenge when patient groups have a relatively low current IQ. Whilst some studies matched for intellectual ability on the basis of pre-morbid reading IQ, this is not acceptable for neurologically impaired groups. The majority of group studies have employed verbal and visual test material, a procedure which should be followed consistently alongside the routine inclusion of both recall and recognition tests. Encouragingly, initial learning was equated and floor and ceiling effects were avoided in many cases, however consideration should be given to the most appropriate means of achieving this. The majority of studies also endeavoured

to prevent rehearsal; however it is difficult to ascertain the success of the methods employed. The most reliable option for future studies may be to specifically select stimuli that are difficult to rehearse. None of the group studies included a filled delay before immediate recall, highlighting a clear indication to adopt this practise in future.

To conclude, existing studies of ALF are fraught with methodological difficulties heralding the drive to confirm that ALF is more than a by-product of experimental designs. With this is mind the field would benefit from the emergence of studies with more robust and comparable methodology. Of most importance is to systematically pilot a range of verbal and visual tests to identify which offer the most reliable measure of long-term forgetting. It is also prudent for researchers to bear in mind the clinical importance of investigating ALF and aim to develop repeatable standardised tests which would eventually be suitable for use in clinical practise.

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Research Report

Accelerated Long-Term Forgetting in people with pre-surgical Temporal Lobe Epilepsy: Development of repeatable tests, a group comparison and case-series analysis

ABSTRACT

Purpose

Existing results regarding accelerated long-term forgetting (ALF) are unclear (with some studies demonstrating ALF and some not) and this may be due to methodological issues. This study aimed to further investigate the existence of ALF in temporal lobe epilepsy (TLE) using improved methodology.

Methods

A repeatable battery of verbal and visual tests was specifically designed to assess forgetting over long-delays. In doing so, key methodological problems were addressed by matching initial learning of TLE and control groups, avoiding floor & ceiling effects as far as possible and minimising possibilities for rehearsal. Using a sample of 7 participants with pre-surgical TLE and 29 healthy controls, recall and recognition performance was assessed at immediate, 30-minute and 1-week delays.

Results

Rates of forgetting were compared using a combination of individual and group analysis. Results evidenced that when assessed using improved methodology, some people with TLE show clear ALF, some show forgetting over short delays and some have intact memory.

Discussion

The considerable individual variation in the forgetting profiles of people with TLE highlights that group studies may not be the most appropriate methodology with which to investigate ALF. The reasons for this heterogeneity could be the focus of future research.

Key Words: Accelerated long-term forgetting, forgetting rates, epilepsy, memory

INTRODUCTION

Memory difficulties are frequently observed in people with temporal lobe epilepsy (TLE). This reflects the direct involvement of memory-related brain structures, including the hippocampus in seizure activity. The exact reason for memory problems in TLE is often unclear as there are many factors which could interact to affect memory function including seizure activity (Jokeit et al., 2001), underlying brain pathology (Lencz et al., 1992), anticonvulsant medication (Jokeit et al., 2005), epilepsy surgery (in which part of the temporal lobe is removed (Gleissner et al., 2004)) age of onset (Lespinet et al., 2002) and psychosocial factors (Elixhauser et al., 1999) such as raised levels of anxiety and depression (Thompson & Corcoran., 1992).

While it is well established that TLE may cause deficits on neuropsychological assessments of memory routinely used in clinical practise (Hermann et al., 1997), many people with TLE report everyday memory problems which are not detected by standardised tests (Thompson & Corcoran, 2002). Standardised clinical assessments of memory typically only test at delays of up to 30-minutes (e.g. Wechsler, 1997). However, recent research has highlighted that some people with TLE perform within normal limits after this time yet display abnormally fast forgetting thereafter. It has been postulated that this phenomenon may be explained by a novel form of memory impairment termed accelerated long-term forgetting (ALF; Butler et al., 2007) whereby acquisition and initial consolidation of long-term memories is intact, but an extended period of consolidation required for long-term maintenance of the memories is disrupted. Of note, other authors (Kapur et al., 1997; Mayes et al., 2003) have named this phenomenon long-term amnesia, however for ease of comprehension only the term ALF will be used hereafter.

Accelerated forgetting has generally been taken to indicate a failure in the consolidation of memories. 'Consolidation' refers to the hypothetical processes that stabilise a memory trace within long-term storage so that it can be retrieved later. Whilst consolidation may continue for weeks, months or even years (Squire & Alvarez, 1995) it is generally assumed that its efficacy can be evaluated after relatively short delays. The majority of existing research on forgetting has therefore been concerned with testing memory over short periods. The predominant focus has been on people with classical amnesia which refers to the partial or total loss of memory over short delays associated with neuropathology to the medial temporal lobes and related brain structures (e.g. Aggleton & Brown, 1999).

There are several case studies of people who show intact memory over short delays of up to 30-minutes, followed by rapid forgetting over longer delays of up to six weeks (Kapur et al., 1997; Lucchelli & Spinnler, 1998; Mayes et al., 2003; O'Connor et al., 1997). Although the majority of participants had TLE in common, their aetiology was complicated by other factors such as closed head injury (Mayes et al., 2003), paraneoplastic limbic encephalitis and high seizure frequency (O'Connor et al., 1997), and late onset seizures with no identifiable cause (Kapur et al., 1997; Lucchelli & Spinnler, 1998). These results may therefore reflect other aspects of neuropathology, rendering conclusions difficult to generalise to more typical cases of TLE. Furthermore, there is one study reporting ALF in a person with no documented seizures (De Renzi & Lucchelli, 1993).

A number of group studies have investigated the possibility that ALF may be a characteristic of TLE more generally; however results have been mixed (see Bell & Giovagnoli, 2007 and Butler & Zeman, 2008 for reviews). Some cite evidence for ALF

over days or weeks (Martin et al., 1991; Blake et al., 2000; Manes et al., 2005; Mameniskiene et al., 2006; Butler et al., 2007) whereas others report no evidence of ALF (Giovagnoli et al., 1995; Bell et al., 2005; Bell, 2006).

As discussed, ALF cannot be assessed using existing tools and so it has been necessary for researchers to develop novel instruments and procedures. The discrepancy between existing studies has been attributed to methodological issues (Butler & Zeman, 2008). In particular, groups have not always been well matched for age and IQ possibly confounding measurements of forgetting. In addition, rates of forgetting may be underestimated if initial learning between groups is not equated (see Loftus, 1985). Although the impact of these scaling effects has been debated (see Slamecka & McElree, 1983), studies have been criticised for not overtly considering the potential implications in their interpretations (Paul, 1994).

Those designs incorporating teaching to criterion paradigms to match learning (e.g. Blake et al., 2000) are also confounded by 'overlearning' of stimuli which occurs as a result of repeated presentation. As Bell (2006) argued, overlearning may cause forgetting over short intervals to be underestimated rendering paradigms unable to distinguish whether ALF represents a separate forgetting phenomenon, or a mild consolidation deficit. Furthermore, as highlighted by Isaac & Mayes (1999), studies which matched performance between groups at an immediate delay may be confounded by the risk that performance is partially based on short-term memory (STM) processes. Subsequent retrieval failures may therefore represent a disruption in the transfer to long-term memory as oppose to forgetting. Assessment of forgetting rates may also be confounded by ceiling and floor effects because there is no scope to measure improvement or decline and so the true group mean cannot be ascertained.

Many existing studies of ALF are also limited by their inability to comment on the relationship between laterality of seizure focus and material-specificity having either neglected to assess both modalities or failed to divide groups by seizure laterality. While laterality of seizure focus can be expected to influence performance on standardised tests, with verbal memory deficits being more pronounced in left-sided TLE and (although less reliably) non-verbal memory being more affected in right-sided TLE (Hermann et al, 1997), in ALF, the relationship remains unclear. For instance, Blake et al. (2000) used a verbal test and found evidence of ALF in left but not right-sided TLE. However, Martin et al. (1991) utilized a verbal test and found no difference between left-sided and right-sided TLE groups. Evidence is also inconsistent regarding whether recognition memory is affected by ALF in addition to recall (Butler & Zeman, 2008), and again many studies have neglected to test both.

Reflecting on the point of Caramazza & McCloskey (1988, p.519) that, "If advances in theory are to be sustainable they must be based on unimpeachable methodological foundations," it remains to be confirmed whether ALF is a genuine phenomenon associated with TLE or a by-product of methodology. Endeavouring to investigate ALF using methodologically sound studies is important both clinically and theoretically. Clinically, memory deficits associated with epilepsy are known to have a major impact on quality of life (Giovagnoli & Avanzini, 2000). As noted by Blake et al., 2000, measures which assess forgetting over long delays have the potential to offer a unique contribution to clinical assessment. Most current methodologies depend on the element of surprise to minimise the confounding effects of rehearsal. This means that people can only be tested once highlighting the need for repeatable tests to be developed. Capturing ALF objectively will be critical to help guide clinical treatment and care. For instance, there is some evidence to suggest that rehearsal (Mayes et al., 2003) and

repeated recall (Jansari et al., 2010) may attenuate its effects. Therefore, people found to be affected by ALF may benefit from support to use rehearsal and relearning strategies to enhance consolidation.

Theoretically, this pattern of forgetting has implications for the neural basis of memory as it suggests that despite normal initial learning and consolidation, memories remain vulnerable to disruption (Mayes et al., 2003). To account for this, an extended process of memory consolidation has been presented as a possible explanation (Blake et al., 2000, Kapur et al., 1997). Squire & Alvarez (1995) make the distinction between 'fast' and 'slow' long-term memory consolidation processes. The 'fast' consolidation process is thought to be mediated by medial temporal lobe structures including the hippocampus. If subtle structural damage within the medial temporal lobes leads to a functional disconnection between hippocampal and cortical systems and prevents memories from becoming established during the 'fast' process, then ALF may represent a mild form of amnesic syndrome which goes undetected by standardised tests. The 'slow' consolidation process is thought to depend on a stable environment in the temporal neocortex to allow for repeated and synchronous activation of hippocampal-neocortical connections. This theory is consistent with the hypothesis that ALF is the result of a failure in the slow transfer of information into neocortical storage sites either because structural neuropathology within these sites prevents memories from becoming established or because transfer to them is disrupted by epileptic activity (e.g. Kapur et al., 1997).

Although it has been postulated that ALF may be the result of structural pathology and/or seizure activity (Butler & Zeman, 2008), this remains to be confirmed. With the underlying factors not yet established, the heterogeneity of people with TLE with

respect to seizure activity, structural damage, anticonvulsant medication and demographics must be considered. If it is argued that group averages only make sense with homogenous groups (Caramazza, 1986), then it seems inappropriate that people with TLE are grouped together for comparison. Indeed, the heterogeneity within neurological populations has resulted in case studies being particularly important within the general field of neuropsychology. It is however important to validate findings from case studies with evidence from other studies demonstrating comparable impairments in similar participants (Goldberg, 1995). As suggested by Bell & Giovagnoli (2007), this study therefore analysed data at the group and individual level. To facilitate this, normative data from a large control sample was gathered for the group comparison, from which data of age-matched sub-groups were drawn for individual analysis.

Study Aims

The primary aim was to further investigate the existence of ALF in TLE using improved methodology. Using a combination of group and single case-series analysis, the aim was to provide a detailed comparison of the forgetting rates of people with TLE and healthy controls.

To address the limitations in previous experimental designs, a prerequisite aim was to develop more robust verbal and visual memory tests (comprising both recall and recognition paradigms) to assess forgetting over long delays. To account for the clinical and theoretical need for repeatable tests, an additional aim was to construct two parallel sets and test their utility through assessing long-term forgetting in a pre-surgery TLE group. In attempt to preclude the methodological issues that have confounded the interpretation of previous studies, groups were matched as closely as possible, initial learning was equated using a multiple presentation procedure (Isaac & Mayes, 1999)

and experimental tests were piloted to avoid floor and ceiling effects as far as possible. In addition, the potential for rehearsal was minimised and filled delays preceded immediate testing to ensure information had been stored in long-term memory.

Hypotheses

Using improved methodology:

1. Participants with TLE will show ALF in comparison to controls.
2. Individual participants with right-sided seizure onset will show a material-specific form of ALF on visual memory tests.
3. Individual participants with left-sided seizure onset will show a material-specific form of ALF verbal memory tests.
4. Repeated recall of stimuli will result in attenuation of ALF
5. Epileptic activity during the long-delay period will compromise memory consolidation and therefore participants who experience seizures will show more pronounced ALF over one week than people who do not experience seizures.

METHOD

The study was conducted in the Clinical Psychology Unit, part of the University of Sheffield and in clinics at the Northern General and Royal Hallamshire Hospitals.

The South Yorkshire Research Ethics Committee reviewed and approved this study (see Appendix B). All participants gave informed consent before participating.

Participants

TLE participants

The study included 7 participants (3 male, 4 female) with a diagnosis of TLE who were being considered for epilepsy surgery (individual characteristics are presented in Table 1). This sample represents the total number of people who were enrolled on the Epilepsy Surgery programme at the Royal Hallamshire Hospital in Sheffield during the recruitment period, fulfilled inclusion and exclusion criteria and were willing to take part. Suitable participants were identified by a Consultant Clinical Neuropsychologist.

Inclusion criteria specified that participants: (1) had a diagnosis of TLE, (2) were aged between 18 and 75 years old, (3) had English as a first language, (4) had a Full Scale IQ (FSIQ) >80 on Wechsler Adult Intelligence Scale –3rd Edition (WAIS-III; Wechsler, 1997), (5) had no other neurological conditions or psychiatric illness.

Diagnoses of TLE had been confirmed on the basis of Electroencephalography (EEG) evidence of epileptiform activity, MRI evidence of focal abnormalities, semiology or a combination of these factors. Two participants (TLE2, TLE3) were post-ictal at the time of assessment, meaning that they reported experiencing a seizure in the preceding 24 hours.

Control Participants

The control group consisted of 29 participants (11 male, 18 female) who had been recruited through the email systems of Sheffield Teaching Hospitals and The University of Sheffield. Demographic data and comparisons between groups can be viewed in Table 2.

Independent samples t-tests were used to compare TLE participants and healthy controls on variables thought to influence forgetting (see next section for the tests on which these scores were based). The groups did not differ with regard to age, years in education or levels of anxiety. There was a significant difference between the reading-score derived IQ (a measure of current IQ) of the control group and current FSIQ of the TLE group; the controls typically having a higher IQ (range = 95-114) compared to TLE participants (range = 82-110). A significant difference in levels of depression was also revealed with the TLE group typically having higher levels (range = 2-8) compared to controls (range = 0-9). Of note, the scores of only one TLE participant and one control reached mild clinical levels.

Table 1. Characteristics of TLE Participants

ID	Sex	Age (years)	Education (years)	FSIQ	Age of onset	Duration (years)	Seizure frequency	Seizure types	MRI	Seizure onset EEG	No. of AEDs
TLE1	M	41	11	110	2	39	4-6 monthly	CPS, GTCS, Aura	Left MTS	Left	2
TLE2	F	41	13	82	9 months	40	10-15 monthly	SPS, CPS, GTCS	Left MTS	Left	3
TLE3	F	57	10	99	47	10	6–7 daily	Auras, GTCS	Left amygdala abnormality, left CD	Left ?frontal semiology	1
TLE4	M	54	10	87	7 months	53	7 monthly	not classified	<Right HC volume	Right	3
TLE5	F	21	17	92	Diagnosed age 17	4+	5-7 monthly	Auras, SPS, CPS, GTCS	Right MTS	Right	2
TLE6	F	42	16	108	24	18	Every 10-28 days	SPS, CPS	Right HCS	Right	2
TLE7	M	20	11	85	19	2	1 monthly	CPS	Right MTS	Right	1
Means (SD)	57% M	39.43 (14.43)	12.57 (2.89)	94.71 (11.2)	15.76 (16.84)	27 (19.92)	32.8	Mixed	3 left-sided onset, 4 right-sided onset		2 (0.76)

MTS = mesial temporal sclerosis; HC = hippocampus; HSC = hippocampal sclerosis; CD = cortical dysplasia; SPS = simple partial seizure; CPS = complex partial seizure; GTCS = generalised tonic clonic seizure; AEDs = antiepileptic drugs

Table 2: Participants Demographics: means and standard deviations

	Group		T-test comparisons	
	TLE	Controls	*t*	*p-value*
N	7	29		
Gender (M/F)	3/4	11/18		
Handedness (R/L)	4/1 (2 ambidextrous)	24/4 (1 ambidextrous)		
Age	39.43 (14.43)	40.76 (14.76)	-.215	0.831
IQ	94.71 (11.19)	107.69 (5.06)	-2.994	0.022*
Education (years)	12.57 (2.89)	15.14 (3.43)	-1.83	0.08
Anxiety (HADS)	8.57 (5.47)	5.90 (3.71)	1.56	0.128
Depression (HADS)	4.71 (1.98)	2.38 (2.30)	2.58	0.014*

**p<0.05*

Measures

Copies of the measures used are included in Appendix C.

Measures used to match TLE participants with controls:

The Wechsler Test of Adult Reading (WTAR: Wechsler, 2001)

This measure was administered to estimate premorbid intellectual ability in the control group on the presumption that pre-morbid and current IQ should be the same in healthy participants. The measure provides an estimated FSIQ which was compared to that of TLE participants. The utility of this method relies on strong correlation between reading ability and intellectual functioning in healthy people.

The Wechsler Adult Intelligence Scale – 3rd Edition (WAIS-III, Wechsler, 1999)

The TLE group had completed this measure within the preceding 12 months which provided information about current intellectual functioning. Results were used to ensure that participants current FSIQ was above 80 and to compare intellectual functioning with the control group.

Standardised Neuropsychological Measures:

A comprehensive neuropsychological assessment had been completed for each TLE participant by the Epilepsy Service as part of their preparation for epilepsy surgery. Depending on which test had been administered, the results of the Adult Memory and Information Processing Battery (AMIPB) or the BIRT Memory and Information Processing Battery (BMIPB) were used in individual analysis to identify any difficulties in memory for verbal or visual material over short delays.

Assessments of Long-Term Forgetting:

Two parallel tests comprising verbal and visual material were specifically designed to assess forgetting over long delays. The materials described below are the result of extensive piloting to address methodological problems. Two sets (set A; set B) were created to afford the future possibility of reassessment. To confirm sets were matched for difficulty, all control participants were assessed using both sets. For further details about the test development process refer to Appendix D.

<u>Visual Scenes Test</u>

Two visual tests (set A; set B) were developed using a pool of 618 colour photographs which were downloaded through Google images or selected from personal photograph albums. The tests were partly based on the Family Pictures subtest of the Wechsler Memory Scale – III (Wechsler, 1997) and on the visual scenes test created by Muhlert (unpublished PhD thesis). The tests were created using Microsoft PowerPoint and presented on a PC laptop.

- Recall

Eighteen photographs were designated as recall scenes as they featured prominent objects and could be assigned a verbal label based on their content e.g. 'The Bakery Scene'. It was ensured that each recall scene contained at least 6 salient foreground items; if necessary, additional items were added using Microsoft Photoshop. To guard against participants gaining marks by chance, the images added were not necessarily associated with the scene name or background. Nine recall scenes were randomly allocated to each set.

Each scene was tested only once resulting in three scenes being tested at each delay (45-seconds, 30-minutes, and 1-week). Recall was assessed on the basis of three types of information: item recall which assessed whether the foreground items were remembered (maximum 6 points per scene), spatial recall which assessed whether items were remembered in the correct location (maximum 6 points per scene) and descriptive recall which assessed whether the characteristics of the item were remembered (maximum 12 points per scene; 2 per item correctly recalled).

- Recognition

The remaining 600 photographs were randomly allocated to set A or B. The 300 photographs in each set were numbered randomly from 1 – 300. Every even numbered photograph was designated as a recognition target, and every odd numbered photograph was designated as a foil (thus 150 targets and 150 foils). Three matched recognition tests were then created for each set, each containing 100 items (50 targets, 50 foils). Targets were distributed evenly throughout the beginning, middle and end sections of the initial presentation.

Story Recall & Recognition

Verbal memory was assessed using an existing set of six stories devised by Isaac & Mayes (1999). The stories had been matched for difficulty and each contained 20 units of information based around a different theme. Three stories were allocated to set A and three to set B. Presentation was standardised by pre-recording the stories into a Windows Media Audio File and playing them to participants through a PC laptop.

At test, participants were required to recall as much about the story as possible. To score recall, one point was awarded for each unit of information recalled exactly or inferred in different words. Recognition of each story was assessed using a series of twelve forced-choice questions each with four alternative answers (one correct, three similar foils) from which the participants had to pick the correct one. The position of the correct answer varied between questions and occurred equally often in each position.

Long Term Memory Questionnaire

A brief questionnaire was administered to gather information about participants' perceived memory problems. The questionnaire asked whether participants believed they had memory problems (yes/no). If they responded yes, they were asked to indicate the time period over which they forget information.

Mood Assessment:

The Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983):

This is a widely used 14 item self report questionnaire containing 2 subscales assessing anxiety and depression with good internal validity and test-retest reliability. A raw

score of 8-10 indicates mild cases of anxiety and depression alike, 11–15 indicates moderate cases and 16 or above indicates severe cases (Snaith & Zigmond, 1994).

Seizure Activity:

TLE participants were asked to complete a seizure diary during the week delay. This recorded the seizure type, date and time it occurred. Further information about seizure type, seizure frequency, age of epilepsy onset, EEG recordings, MRI evidence of focal abnormalities and current medication was accessed from medical files with the participants' permission.

Procedure

Testing took place over two sessions spaced one week apart. For their convenience, TLE participants were offered appointments in their own home. The presentation order was counterbalanced such that half received set A, and half set B. The first session was used to present the stimuli and test recall and recognition immediately and after 30-minutes. During the 30-minute delay, all participants completed the HADS, WTAR and Memory Questionnaire during which time TLE participants were also provided with a seizure diary. To avoid confounding repeat assessments, participants were routinely informed when their memory would be tested again. The second session was used to assess forgetting following a week delay.

Visual Scenes

A practice trial preceded presentation of the experimental scenes. This consisted of one recall scene and eight recognition scenes which were presented according to the same procedure as the experimental scenes.

The visual scenes were presented in consecutive blocks each containing eight recognition targets interspersed with blank screens followed by one recall scene (see Figure 1 for timings). Each recall scene was divided into quarters which were outlined one at a time followed by the whole scene. Each recognition picture was shown once and each recall scene was shown twice (1-9, then 1-9 again). The presentation order was identical between participants; however the order of recall and recognition tests at each delay was counterbalanced.

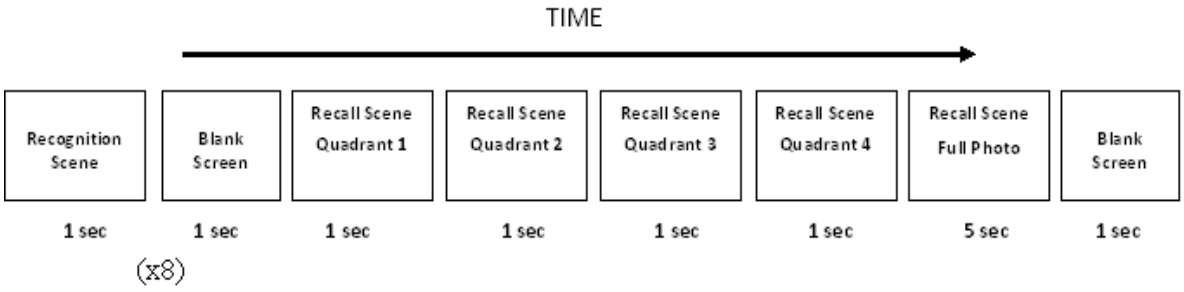


Figure 1. Order of presentation of recognition and recall scenes in the visual scenes test

To ensure encoding, participants were asked to name something in each picture. The following instructions were presented on a blank screen and read aloud by the experimenter:

"You are about to see lots of pictures; your recognition for which will be tested. Each picture will appear for one second. During this time, you should name an object in the picture. So, if the picture has a car in it, just say "car."

Some pictures appear five times in a row. One section will be outlined at a time - please name something in each of the outlined parts. These scenes have names. Read these aloud and remember them. You will later be asked to recall the parts of these pictures in detail."

To match initial learning as closely as possible, a multiple-presentation procedure was employed so each TLE participant was shown the initial presentation twice. To ensure immediate recall was based on long-term memory processes, the test was preceded by a 45-second interference task which required participants to judge whether a set of two digit numbers were odd or even. The following instructions were given:

"Before we continue, I would like you to judge whether the numbers which appear on the screen are odd or even."

To test recall at each delay, participants were asked questions about three scenes. Having been cued with the name of each scene, participants were asked to name what was in the picture (item recall), specify the location of items on the recall grid (spatial recall) and describe their appearance (descriptive recall). In the recognition component, participants were given the following instructions:

"You will now see a series of pictures. You need to decide whether or not you have seen the picture before. Answer yes or no."

Stories

To match initial learning as closely as possible, a multiple-presentation procedure was employed so each story was played once to control group participants and twice to TLE group participants. To prevent rehearsal of the target stories and assess the effect of repeated recall on forgetting, the first story was recalled at each delay. One of the other two stories was recalled only at the short delay and the other one only at the long delay ('Short-Delay Story': 30-minutes; 'Long-Delay Story': 1-week). Only data from the

last two stories were used to assess forgetting. Data from the first story were used to assess the effects of rehearsal and repeated recall.

Participants were given the following instructions:

"I am going to play you three stories, one at a time. I want you to listen to each story and remember what happens in it. After each story ends you will be asked to tell me as much as you can remember about the story. Pay special attention to the first story as I will be most interested in your memory for this one and will ask you about it again."

Immediate recall was assessed after a 20 second unfilled delay using the following instructions: "*Now tell me as much as you can remember."*

30-minute delay: "*Now, think back to the stories you heard earlier. I would like you to tell me as much of the first and second stories as you can remember."*

1-week delay: "*Now, think back to the stories you heard last week. I would like you to tell me as much of the first and last stories as you can remember."*

Recognition was assessed after recall using the following instructions:

"I am now going to ask you twelve questions about the story. You will be given four possible answers to each question from which I would like you to select the correct one."

Data Analysis

Group Analysis

Data were analysed using SPSS 18.0 for windows. Prior to statistical analysis the data were checked to ensure normal distribution and the absence of ceiling effects. If the distribution was skewed, appropriate log transformations were applied. Outlying data were retained as removing unexpectedly poor control data would have biased results towards Type I error. Where large sets of comparisons were made, Bonferroni adjustments were applied to the alpha level to protect against the likelihood of Type I errors. Alpha levels were set at 0.05 unless otherwise reported.

Case Series Analysis

Each TLE participant was matched as closely as possible for age and IQ with a subset of the control group. Two forgetting scores were calculated for each dependant variable (Time 1: immediate - 30-minutes; Time 2: 30-minutes - 1-week). The results corresponded to the units of information forgotten.

To enable comparison between each TLE participant and their respective controls, a formula described by Crawford & Howell (1998) and Crawford & Garthwaite (2002) was used (see Appendix E). The authors' refer to the method as a modified independent-samples t-test which is suitable for comparing an individual's score against the norms derived from small samples.

The assumptions of normal distribution still apply; however the method's robustness in the face of violations has been demonstrated (Crawford et al., 2006). In cases where there were serious concerns about the shape of the control distribution, a square root or log-transformation was applied to both data before analysis. If the small sample size

and granularity of the data impeded ability to ascertain the direction of the skew and decide on an appropriate transformation, or if transformation results were unsatisfactory, the authors' suggestion to adopt a more conservative alpha level of 0.02 was followed. Alpha levels were set at 0.05 unless otherwise reported.

RESULTS

Of note, 'immediate delay' hereafter refers to 45-seconds and 20-seconds for visual and verbal tests respectively.

Group Analysis

Independent-samples t-tests were used to compare the performance of TLE participants and Controls at the immediate delay to evaluate whether initial learning was adequately matched. As is evidenced in Table 3, there were no significant differences between groups. Initial learning was therefore considered to have been successfully equated.

Table 3: Performance on experimental tests at immediate delay

	TLE Mean (SD)	**Controls** Mean (SD)	*p-value*
N	7	29	
Visual Tests			
Item Recall	13.86 (4.3)	15.31 (2.38)	0.417
Spatial Recall (*s*)	6.38 (1.04)	6.70 (0.57)	0.458
Descriptive Recall (*d)*	71.66 (18.6)	79.18 (7.85)	0.332
Recognition Sensitivity (*d'*)	3.1 (0.92)	3.81 (0.5)	0.093
Verbal Stories			
'Short-Delay Story' Recall	11.43 (4.86)	12.55 (3.22)	0.460
'Short-Delay Story' Recognition	9.71 (1.38)	9.72 (1.77)	0.989
'Long-Delay Story' Recall	12.14 (5.18)	12.03 (3.05)	0.946
'Long-Delay Story' Recognition	9.86 (1.21)	9.83 (1.86)	0.959

Due to group differences in current intellectual ability, performance of the TLE and Control groups across all experimental tests (visual scenes item recall, spatial recall and descriptive recall, visual scene recognition, 'short-delay story' recall and recognition and 'long-delay story' recall and recognition) were entered into a multivariate repeated-measures analysis of covariance (MANCOVA) with IQ as a covariate. The factors were delay (immediate, 30-minute, 1-week) and group. Further analysis on individual tests was contingent upon the multivariate analysis rejecting the null hypothesis. The MANCOVA found a significant delay by group interaction (Pillai's trace=0.853,

$F(16,18) = 6.521$, $p<0.001$) which suggests that forgetting differed significantly between groups. Therefore, forgetting rates between groups on individual experimental tests were compared using a mixed between-within 2 x 3 repeated measures ANCOVA with factors of group (2 levels: TLE, Controls) and delay (3 levels: immediate, 30-minute, 1-week) using IQ as the covariate.

ANCOVAs revealed that IQ did not have a significant main effect or relationship with the dependant variables when analyzed separately. Given the dubious assumptions made by ANCOVAs and the problem associated with using it as a matching technique (see Adams et al, 1985); the analyses were re-run without it. The following results are reported from repeated measures ANOVAs without IQ as a covariate. Greenhouse-Geisser correction was applied for non-sphericity where appropriate.

Visual Scenes Recall

Item Recall

A repeated measures ANOVA comparing the performances of the two groups across all three delays found a significant main effect of delay ($F(1.71, 58.26) = 67.537$, $p<0.001$). There was no main effect of group or delay by group interaction. This indicates a comparable pattern of forgetting between groups with TLE participants and controls recalling fewer items over time (see Figure 2).

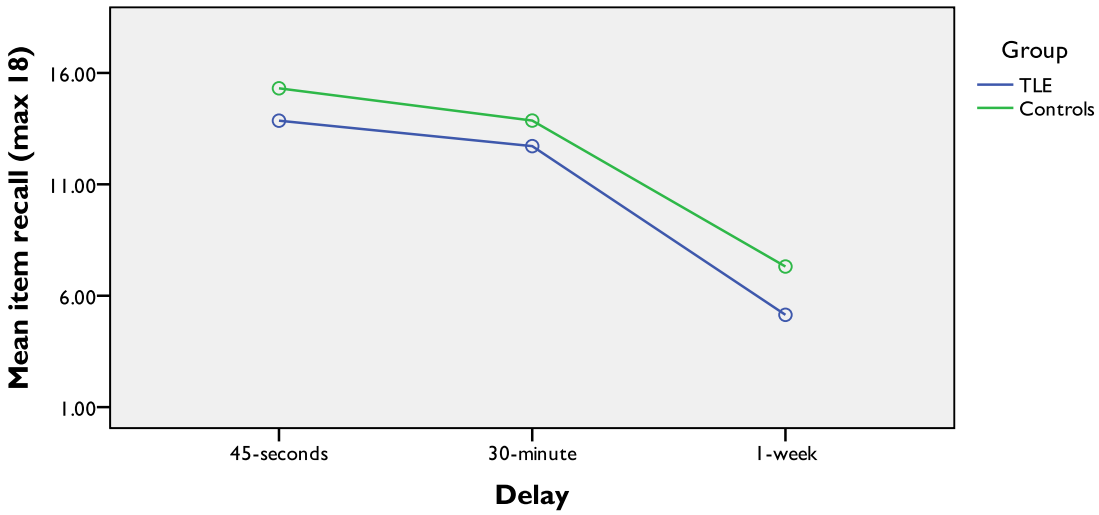


Figure 2. Mean item recall of TLE and Control groups on the visual scenes recall test.

Spatial Recall

Spatial recall was scored using a corrected measure of discrimination which takes into account the probability that an item is discriminated correctly by chance (see Hunkin et al., 1994). To compensate for this, Hunkin et al.'s discrimination score (*z*) was used (see Appendix E). To avoid confusion with standard z scores, this score will be referred to as *s* hereafter.

Using *s* scores, a repeated-measures ANOVA compared performances of the two groups across all three delays and found a significant main effect of delay ($F(1.35, 46.04) = 75.73$, $p<0.001$, a significant main effect of group ($F(1,34) = 5.406$, $p=0.026$) and a significant delay by group interaction ($F(1.35, 46.04) = 6.954$, $p=0.006$). Contrasts between pairs of delays found no significant delay by group interaction between 45-seconds and 30-minutes but a significant delay by group interaction between 30-minutes and one week ($F(1,34)=7.527$, $p=0.010$). This indicates that the TLE group demonstrated more rapid forgetting of spatial information between 30-minutes and 1-week than controls (see Figure 3).

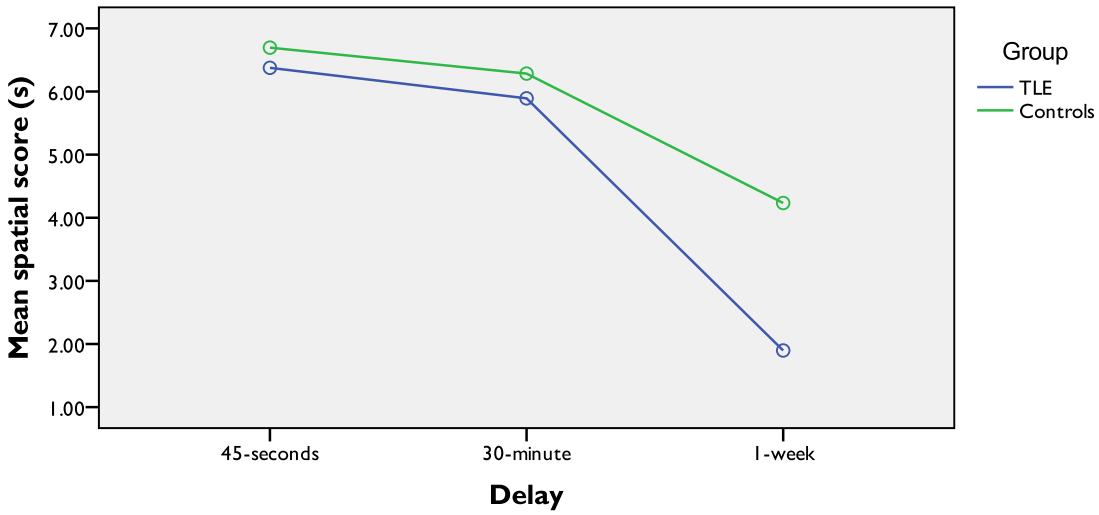


Figure 3. Mean spatial discrimination memory score *(s)* of TLE and Control groups on the visual scenes recall test.

Descriptive Recall

To account for the differences in the number of items recalled, a corrected measure of descriptive recall *(%d)* devised by Muhlert (unpublished PhD thesis) was applied (see Appendix E for details). Using this score, repeated measures ANOVA compared the performances of the two groups across all three delays and found a significant main effect of delay ($F(1.64, 55.63) = 23.513$, $p<0.001$), a significant main effect of group ($F(1,34) = 11.339$, $p=0.002$) and a significant delay by group interaction ($F(1.64, 55.63) = 4.618$, $p=0.02$). Contrasts between pairs of delays found no significant delay by group interaction between 45-seconds and 30-minutes but a significant delay by group interaction between 30-minutes and 1–week ($F(1,34)=4.358$, $p=0.044$). This indicates that forgetting of descriptive information was accelerated in the TLE group over the long-delay (see Figure 4).

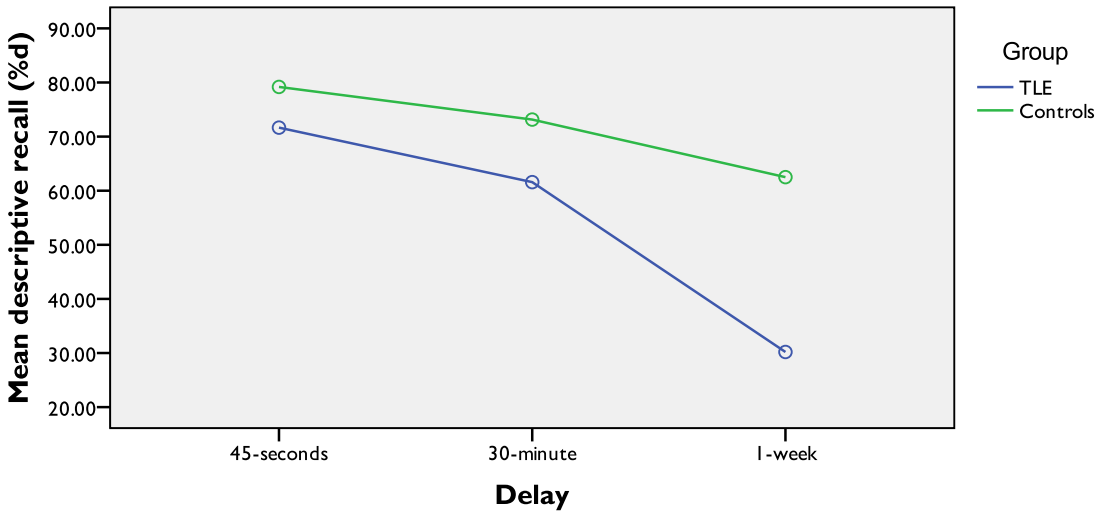


Figure 4. Mean descriptive recall (%d) of TLE and Control groups on the visual scenes recall test.

Visual Scenes Recognition

Visual scene recognition was scored using signal detection theory (see Macmillan & Creelman, 1991). The number of hits and false positives were taken into account by calculating an index of accuracy (d') and an index of bias (b). For further details see Appendix E.

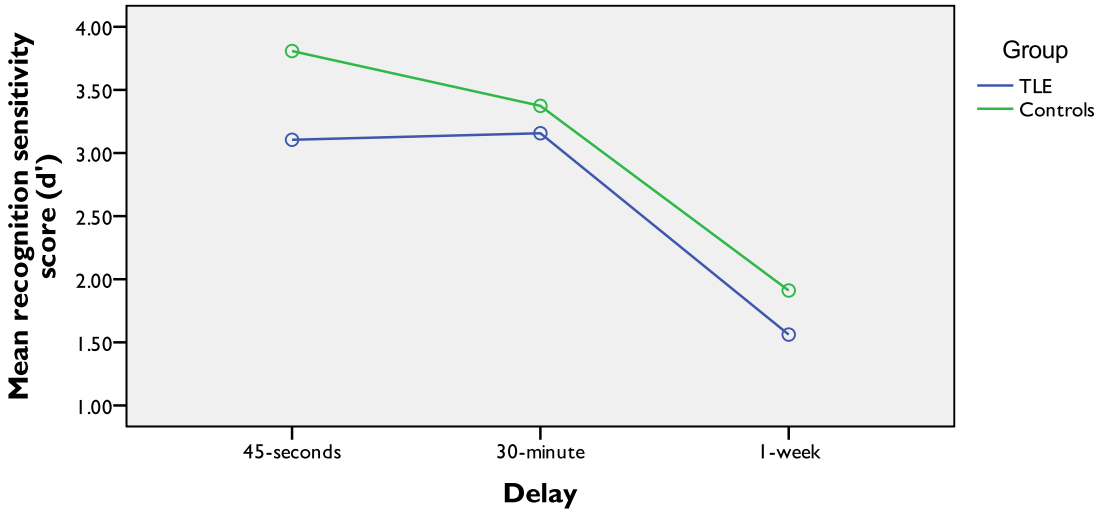
Accuracy

Using *d'* scores, repeated measures ANOVA comparing the accuracy of recognition responses of the two groups across all three delays found a significant main effect of delay ($F(2,68) = 92.877$, $p<0.001$) but no delay by group interaction ($F2,68) = 1.65$, $p=0.200$). The main effect of group was just significant ($F(1,34) = 4.174$, $p=0.049$). This indicates that the recognition response sensitivity of both groups reduced over time (see Figure 5a).

Bias

It has been found that bias rather than sensitivity can differ between groups. Repeated measures ANOVA therefore compared recognition response biases (b) to evaluate the extent participants were biased towards responding 'yes' or 'no' across all three delays. There was a significant main effect of delay ($F(1.57, 53.46) = 18.78$, $p<0.001$) but no main effect of group or delay by group interaction. This indicates TLE participants and controls were increasingly biased towards responding 'No' over time (see Figure 5b).

5a.



5b.

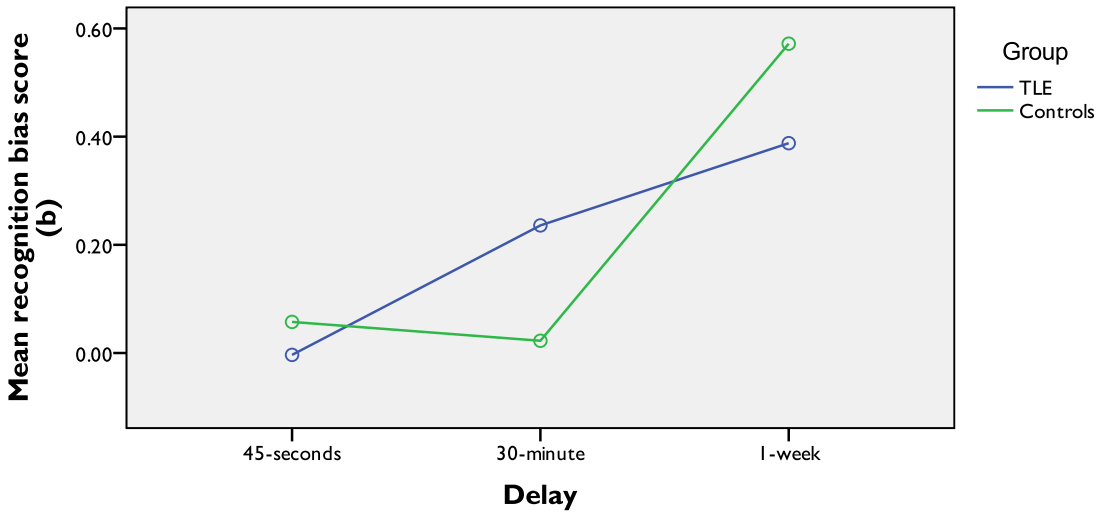


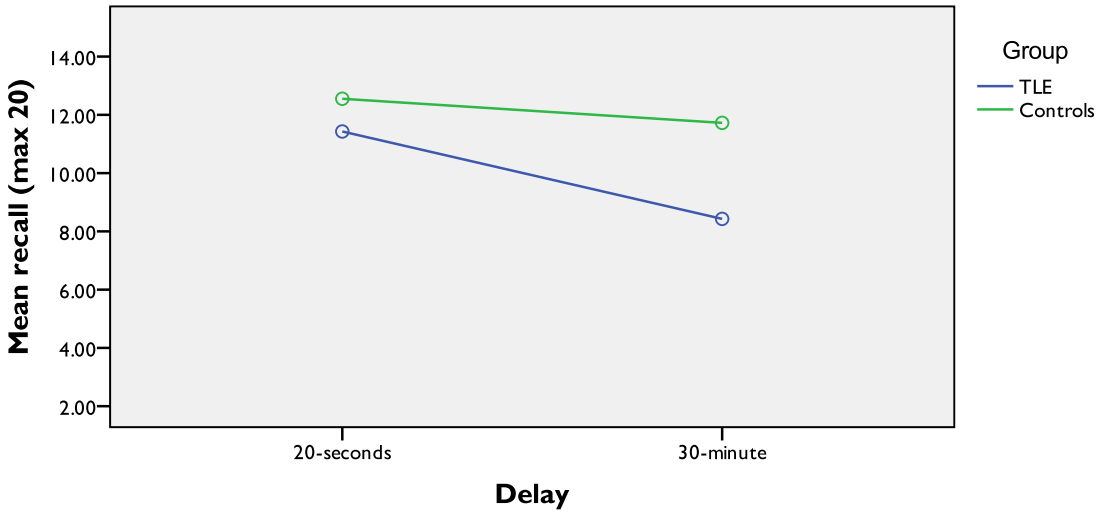
Figure 5: Mean performance of TLE and Control groups on: a. visual recognition accuracy, b. visual recognition bias

Story Recall

The 'short-delay story' was analysed to compare forgetting over 30-minutes. Repeated measures ANOVA compared performances across two delays (20-second, 30-minutes) and found a significant main effect of delay ($F(1,34) = 29.216$, $p<0.001$) and a significant delay by group interaction ($F(1,34) = 9.412$, $p=0.004$). This indicates that the TLE group were already forgetting more rapidly over the short delay (see Figure 6a).

The 'long-delay story' was analysed to compare forgetting between the two groups over one week in the absence of a repeated recall test after 30-minutes. Repeated measures ANOVA compared performances across two delays (20-seconds, 1-week) and found a significant main effect of delay ($F(1,34) = 143.191$, $p<0.001$), a significant main effect of group ($F(1,34) = 4.492$, $p=0.041$) and a significant delay by group interaction ($F(1,34) = 26.014$, $p<0.001$). This indicates that forgetting over the long-delay was accelerated in the TLE group (see Figure 6b).

6a.



6b.

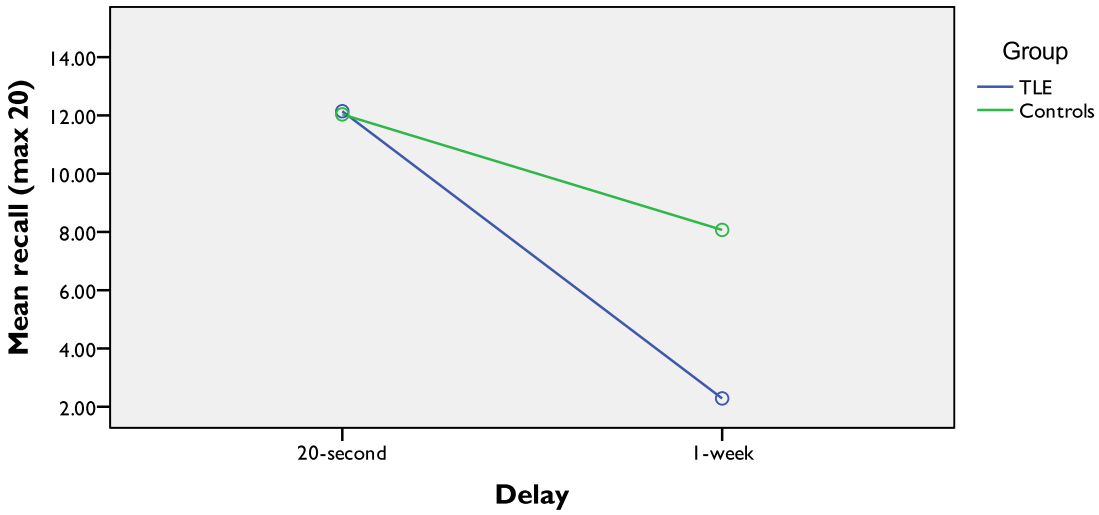


Figure 6: Mean performance of TLE and Control groups on story recall: a. Short Delay b. Long Delay

Repeated Story Recall

To assess the affect of repeated recall at 30-minutes, repeated measures ANOVA compared the performances of the two groups across all three delays and found a significant main effect of delay ($F(2,68) = 47.26$, $p<0.001$), a significant main effect of group ($F(1,34) = 19.32$, $p<0.001$) and a significant delay by group interaction ($F(2,68) = 22.53$, $p=0.003$). Contrasts between pairs of delays found no significant delay by group interaction between 20-seconds and 30-minutes, however the delay by group interaction between 30-minutes and 1-week was approaching significance ($F(1,34)=3.821$, $p=0.059$). This indicates a non-significant trend towards the TLE group forgetting more about the repeated story over both short and long delays (see Figure 7).

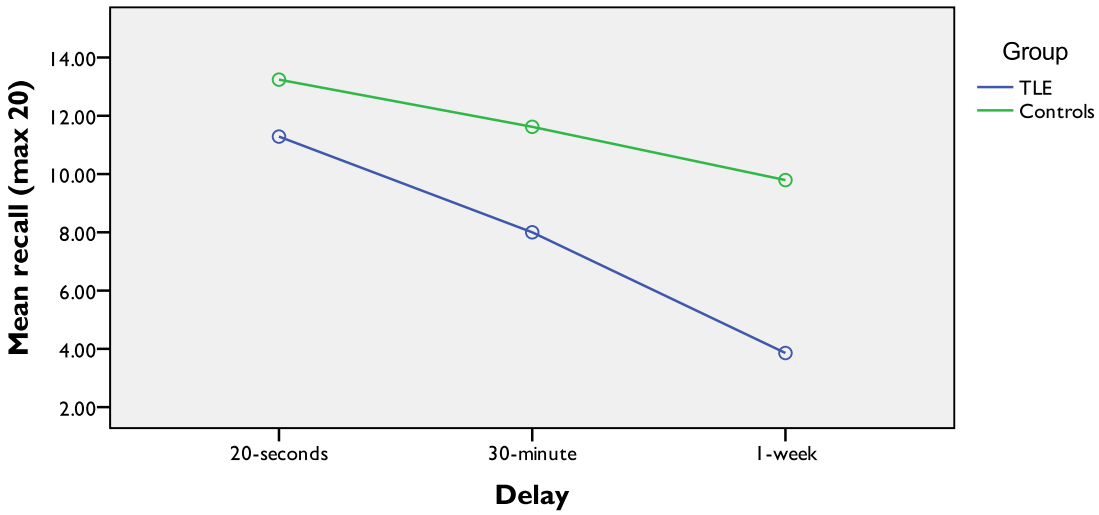


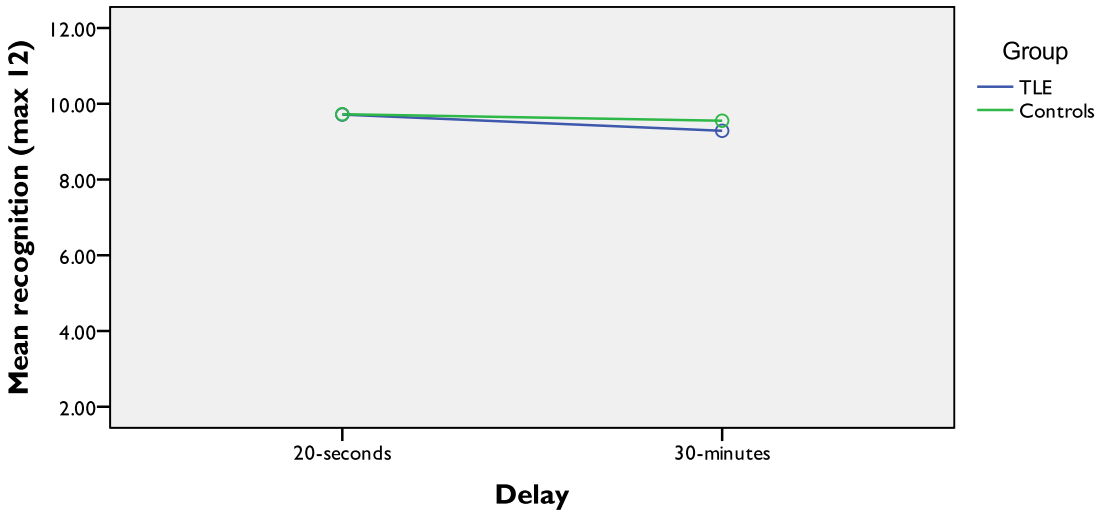
Figure 7: Mean performance of TLE and Control groups on recall of repeated story

Story Recognition

Recognition scores for the 'short-delay story' were compared using repeated measures ANOVA across two delays (20-seconds, 30-minutes). There was no significant main effect of delay, group or delay by group interaction. This indicates that story recognition remained constant and was comparable between groups over the short delay (see Figure 8a).

Recognition scores for the 'long-delay story' were compared using a repeated measures ANOVA across two delays (20-seconds, 1-week). There was a significant main effect of delay ($F(1,34) = 54.653$, $p<0.001$) and a significant delay by group interaction ($F(1,34) = 9.793$, $p=0.004$). This indicates that story recognition was also affected by ALF in the TLE group (see Figure 8a).

8a.



8b.

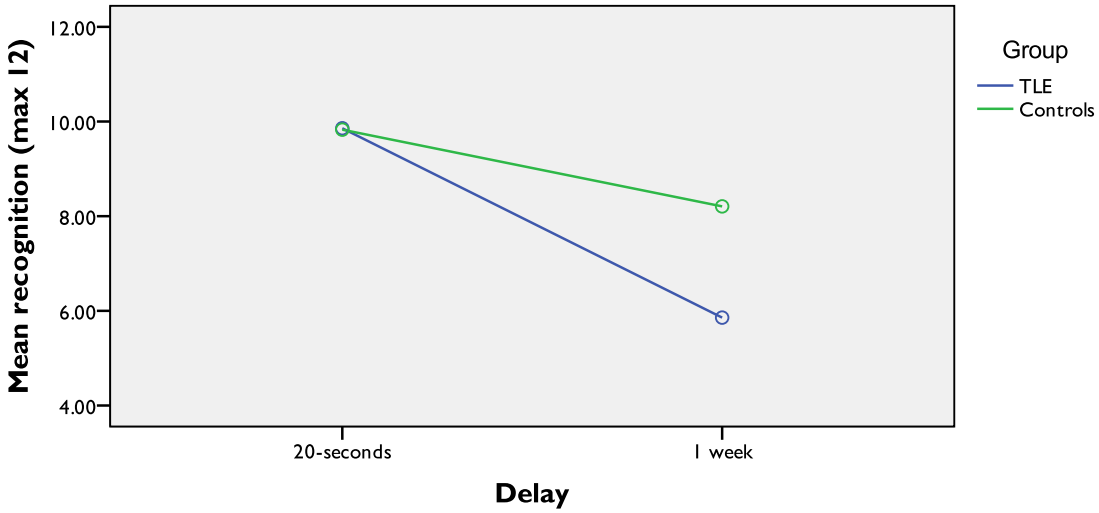


Figure 8: Mean performance of TLE and Control groups on verbal recognition a. Short Delay, b. Long Delay.

Repeated Story Recognition

Repeated measures ANOVA compared the performances of the two groups across all three delays and found a significant main effect of delay ($F(1.442, 49.032) = 19.529$, $p<0.001$, a significant main effect of group ($F(1,34) = 9.534$, $p=0.004$) and a significant delay by group interaction ($F(1.442, 49.032) = 10.552$, $p=0.001$). Contrasts between

pairs of delays found no significant delay by group interaction between 20-seconds and 30-minutes but a significant delay by group interaction between 30-minutes and one week ($F(1,34)=18.095$, $p<0.001$). This indicates verbal recognition was affected by ALF in the TLE group (see Figure 9).

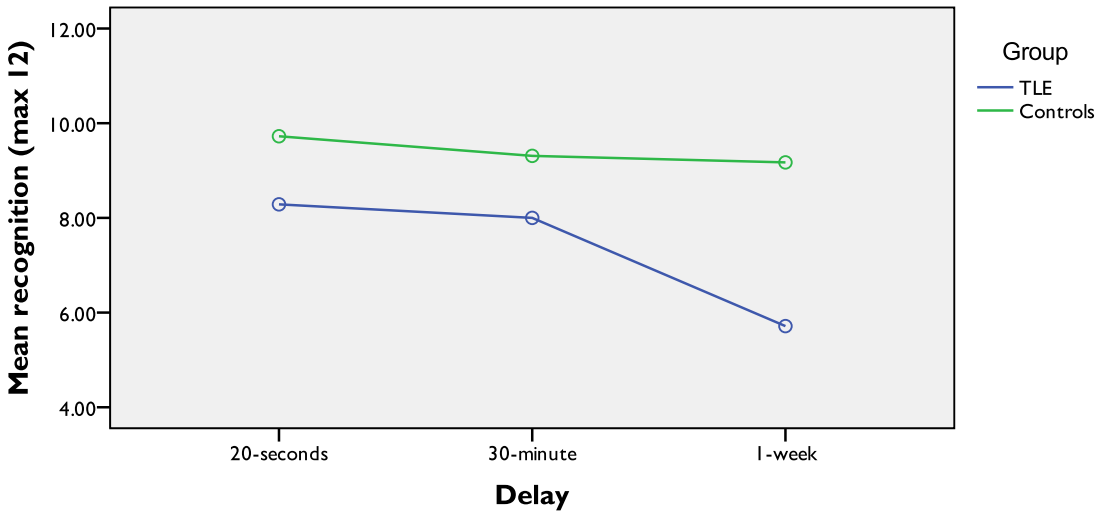


Figure 9: Mean performance of TLE and Control groups on recognition of repeated story

Effects of Seizures

Three TLE participants experienced seizures during the week delay and four were seizure-free. Due to the very small numbers, the different seizure types and frequency were collapsed into two categories (seizure or seizure-free). Mean forgetting scores over the long delay (immediate to 1-week) on all experimental tests were compared. Independent-samples t-tests found no significant differences in forgetting ($p > 0.05$ in all cases).

Perceived Long-Term Memory

All TLE participants and 11 controls reported subjective problems with memory. Only TLE6 and TLE7 reported long-term forgetting over days or weeks. The remaining participants reported accelerated forgetting over minutes or hours. Memory concerns reported by control participants were predominantly related to forgetting over minutes or hours associated with increasing age.

Case-Series Analysis

Given the variability within groups, each TLE participant was compared with a subset of the control group. The reader is directed to Table 1 for demographic data on each individual. Forgetting rates of each TLE participant and the means of their respective control group are presented in tables 4-10.

Left TLE participants

TLE1

TLE1 was matched with 8 healthy controls (7 females, 1 male) for age ($t(7) = 0.145$, $p=0.889$) IQ ($t(7) = 0.207$, $p=0.842$), years in education ($t(7) = -1.559$, $p=0.163$), anxiety ($t(7) = 0.457$, $p=0.662$) and depression ($t(7) = 0.00$, $p=1.00$). Initial learning was matched on all tests ($p>0.05$) with the exception of verbal recall ('short-delay story': $t(7) = 2.35$, $p=0.026$; 'long-delay story': $t(7) = 3.83$, $p=0.003$). Examination of raw scores revealed that he had outperformed the control group.

Examination of scores on the BMPIB indicated that his memory for verbal and visual material over short delays is intact. On visual tests ALF was found on spatial recall ($t(7) = 3.330$, $p=0.006$). On verbal tests, ALF was demonstrated by recall ($t(7) = 4.333$, $p=0.002$) and recognition ($t(7) = 2.111$, $p=0.036$) of the long-delay story. Interestingly,

these results are not consistent with his subjective reports of faster forgetting over short delays.

Table 4: Forgetting scores of TLE1 and control sub-group on assessments of ALF

	TLE1	Control Mean (SD)
N	1	8
Visual Tests		
Item Recall T1	2	2.25 (4.10)
Item Recall T2	7	6.38 (3.46)
Spatial Recall (*s*) T1	0.42	0.59 (1.11)
Spatial Recall (*s*) T2	4.81	4.14 (0.10) **
Descriptive Recall (*d)* T1	16.67	7.04 (11.03)
Descriptive Recall (*d*) T2	19.44	7.55 (16.52)
Recognition Sensitivity (*d'*) T1	-0.30	0.34 (0.84)
Recognition Sensitivity (*d'*) T2	2.39	1.66 (0.62)
Verbal Stories		
Short-Delay Story Recall	3	0.63 (1.51)
Short-Delay Story Recognition	1	-0.13 (0.85)
Long-Delay Story Recall	13	3.25 (2.12)**
Long-Delay Story Recognition	4	1.62 (1.06)*
Repeated Story Recall T1	2	1.13 (3.04)
Repeated Story Recognition T1	0	0.5 (0.53)
Repeated Story Recall T2	3	2.5 (3.89)
Repeated Story Recognition T2	1	0.13 (0.99)

*p<0.05, **p≤ 0.01 T1 = Immediate-30minute, T2 = 30-minute to 1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

TLE2

TLE2 was matched with 8 healthy controls (6 females, 2 males) for age (t(7) = -0.300, p=0.773), years in education (t(7) = -0.161, p=0.877, anxiety (t(7) = 1.256, p=0.249) and depression (t(7) = 1.783, p=0.118). It was not possible to match the control group for IQ (t(7) = -5.533, p=0.001) with controls having a significantly higher IQ (range = 95-114). Initial learning was successfully matched on all tests.

Scores on the AMPIB indicate that her memory for verbal material ranges from below average to average limits and memory for visual material is below average. On visual experimental tests, accelerated forgetting over the long delay was found on tests of item recall (t(7) = 2.14, p=0.035) and descriptive recall (t(7) = 2.923, p=0.011). On verbal

experimental tests, ALF was demonstrated by recall (t(7) = 3.258, p=0.007) and recognition (t(7) = 4.326, p=0.002) of the 'long-delay story'. Her forgetting of the repeated story was significantly faster over the short delay (Recall: t(7) = 1.938, p=0.047; Recognition: t(7) =-2.925, p=0.011) and the long delay (Recognition: t(7) = 2.693, p=0.015).

Table 5: Forgetting scores of TLE2 and control sub-group on assessments of ALF

	TLE2	Control Mean (SD)
N	1	8
Visual Tests		
Item Recall T1	-1	2.5 (4.47)
Item Recall T2	16	6.38 (4.24)*
Spatial Recall (*s*) T1	-0.21	0.67 (1.19)
Spatial Recall (*s*) T2	1.10	1.23 (0.04)
Descriptive Recall (*d)* T1	5.23	12.2 (14.10)
Descriptive Recall (*d*) T2	63.89	8.68 (17.81)**
Recognition Sensitivity (*d'*) T1	-0.75	0.24 (0.60)
Recognition Sensitivity (*d'*) T2	2.11	1.63 (0.52)
Verbal Stories		
Short-Delay Story Recall	1	1.38 (1.06)
Short-Delay Story Recognition	0	0 (0.93)
Long-Delay Story Recall	10	2.63 (2.13)***
Long-Delay Story Recognition	6	1.25 (1.04)***
Repeated Story Recall T1	5	1.13 (1.89)*
Repeated Story Recognition T1	-2	0.75 (0.89)**
Repeated Story Recall T2	5	3.0 (3.46)
Repeated Story Recognition T2	4	-0.25 (1.49)**

*p<0.05, **p<0.02, ***p<0.01 T1 = Immediate-30minutes, T2 = 30-minutes to 1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

TLE3

TLE3 was matched with 10 healthy controls (7 females, 3 males) who were matched for age (t(9) = 0.00, p=1.00), IQ (t(9) = -1.311, p=0.222), years in education (t(9) = -1.018, p=0.335) and depression (t(9) = 0.685, p=0.510). Comparisons between levels of anxiety was approaching significance (t(9) = 2.253, p=0.051) reflecting the severe levels of anxiety reported by TLE3. Efforts to match initial learning were unsuccessful on item recall (t(9) = -2.316, p=0.023) spatial recall (t(9) = -2.488, p=0.017), recognition sensitivity (t(9) = -2.712, p=0.012), repeated story recall (t(9) = -3.101 ,

p=0.006) and recognition (t(9) = -3.258, p=0.005). Examination of means revealed that the TLE3's performance was significantly poorer in these comparisons.

Table 6: Forgetting scores of TLE3 and control sub-group on assessments of ALF

	TLE3	Control Mean (SD)
N	1	10
Visual Tests		
Item Recall T1	4	2.20 (3.16)
Item Recall T2	4	7.2 (4.64)
Spatial Recall (*s*) T1	1.43	0.67 (0.94)
Spatial Recall (*s*) T2	3.46	2.57 (2.37)
Descriptive Recall (*d)* T1	31.25	7.11 (19.22)
Descriptive Recall (*d*) T2	37.50	15.15 (36.99)
Recognition Sensitivity (*d'*) T1	0.58	0.52 (0.62)
Recognition Sensitivity (*d'*) T2	1.40	1.32 (0.29)
Verbal Stories		
Short-Delay Story Recall	3	1 (2.26)
Short-Delay Story Recognition	3	0.6 (1.35)
Long-Delay Story Recall	9	3.7 (3.34)
Long-Delay Story Recognition	3	1.9 (2.13)
Repeated Story Recall T1	5	0.70 (2.67)
Repeated Story Recognition T1	1	0.40 (1.07)
Repeated Story Recall T2	3	1.2 (2.62)
Repeated Story Recognition T2	1	0.4 (0.70)

p>0.05 in all comparisons. T1 = Immediate-30minute, T2 = 30-minute to 1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

Scores on the AMPIB indicate that her memory for verbal material over short delays is impaired. Her ability to learn and retain visual information is variable, but generally intact. On experimental tests there were no significant differences in forgetting rates. Examination of raw scores revealed that performance was at floor at the long delay on item recall, spatial recall, repeated story recall and 'long-delay story' recall. Qualitatively she had only a vague recollection of the learning episode and commented that her responses to recognition questions were guesses. In addition to the presence of floor effects at the long delay and differences in initial learning, these factors are likely to have led to her forgetting rates over short and long delays being underestimated. For this participant it is therefore impossible to conclude with any certainty that

performance at the standard delay was not impaired or comment on the presence or absence of ALF.

Right TLE participants

TLE4

TLE4 was matched with 9 healthy controls (6 females, 3 males) for age (t(8) = -0.627, p=0.548), years in education (t(8)-0.923, p=0.383), anxiety (t(8) = -0.024, p=0.981) and depression (t(8) = 0.949, p=0.370). It was not possible to match the control group for IQ (t(8) = -3.102, p=0.015). The controls had a significantly higher IQ (range = 95-114). Despite efforts to match initial learning, there were significant differences in performance at the immediate delay on visual item recall (t(8) = -2.843, p=0.022), spatial recall (t(8) = -2.895, p=0.020) and repeated story recall (t(8) = -3.874, p=0.005). On visual tests, examination of mean scores revealed that the TLE4's performance was significantly poorer in these comparisons.

Table 7: Forgetting scores of TLE4 and control sub-group on assessments of ALF

	TLE4	Control Mean (SD)
N	1	9
Visual Tests		
Item Recall T1	1	1.78 (3.03)
Item Recall T2	9	8.56 (4.64)
Spatial Recall (*s*) T1	1.05	0.58 (0.90)
Spatial Recall (*s*) T2	4.43	2.95 (2.39)
Descriptive Recall (*d)* T1	15.56	10.47 (13.82)
Descriptive Recall (*d*) T2	44.44	14.35 (38.99)
Recognition Sensitivity (*d'*) T1	0.37	0.33 (0.44)
Recognition Sensitivity (*d'*) T2	1.31	1.36 (0.34)
Verbal Stories		
Short-Delay Story Recall	6	1 (2.29)*
Short-Delay Story Recognition	-1	0.33 (1.32)
Long-Delay Story Recall	4	3.67 (2.50)
Long-Delay Story Recognition	5	1.56 (1.94)
Repeated Story Recall T1	3.87	4.48 (0.30)
Repeated Story Recognition T1	2	0.67 (1.12)
Repeated Story Recall T2	2	0.67 (2.35)*
Repeated Story Recognition T2	3	0.22 (0.67)**

*p<0.05, **p<0.01 T1 = Immediate-30minute, T2 = 30-minute -1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

Examination of scores on the BMPIB indicates that his memory for verbal and visual material at short delays is variable ranging between impaired and average limits. On visual experimental tests there were no significant differences between TLE4 and his respective control group. On verbal tests, he demonstrated accelerated forgetting for the repeated story over the long delay (Recall: t(8) = -1.907, p=0.046; Recognition: t(8) = , p=0.002). Forgetting was also accelerated for the 'short-delay story' (t(8) = 2.071, p=0.036). Examination of raw scores revealed that he performed at floor level after 1-week on tests of item recall, spatial recall, descriptive recall, repeated story recall and 'long-delay story' recall. Recall of the 'short-delay story' was also at floor level.

The observed floor effects coupled with inadequate matching of initial learning may have led to his forgetting rates being underestimated. Overall, these results are variable and are more suggestive of generally poor learning and memory rather than specific hallmarks of ALF. This conclusion is supported by results from standardised memory tests.

TLE5

TLE5 was matched with 7 healthy controls (4 females, 3 males) for age (t(6) = -0.520, p=0.621), years in education (t(6) = 0.585, p=0.580), anxiety (t(6) = 2.002, p=0.092) and depression (t(6) = 1.155, p=0.292). It was not possible to match the control group for IQ (t(6) = -2.72, p=0.035). The controls had a significantly higher mean IQ (range = 92-113). Initial learning was adequately matched on all tests.

Examination of scores on the BMPIB indicates that her memory for verbal and visual material over short delays is intact. On experimental tests, there was no evidence for accelerated forgetting; her performance was comparable with controls on all measures.

This indicates that memory for verbal and visual information over short and long delays is intact.

Table 8: Forgetting scores of TLE5 and control sub-group on assessments of ALF

	TLE5	Control Mean (SD)
N	1	7
Visual Tests		
Item Recall T1	0	1 (1.41)
Item Recall T2	4	5.29 (3.73)
Spatial Recall (*s*) T1	0	0.23 (0.33)
Spatial Recall (*s*) T2	0.90	1.54 (1.32)
Descriptive Recall (*d)* T1	14.71	-1.36 (12.50)
Descriptive Recall (*d*) T2	25.11	8.55 (16.61)
Recognition Sensitivity (*d'*) T1	0	0.56 (0.62)
Recognition Sensitivity (*d'*) T2	1.55	1.42 (0.77)
Verbal Stories		
Short-Delay Story Recall	2	1.43 (1.40)
Short-Delay Story Recognition	2	0.14 (0.69)
Long-Delay Story Recall	7	5 (1.53)
Long-Delay Story Recognition	-1	2 (1.53)
Repeated Story Recall T1	-2	2.71 (4.23)
Repeated Story Recognition T1	0	0.43 (0.53)
Repeated Story Recall T2	4	1.14 (2.12)
Repeated Story Recognition T2	1	-0.29 (1.60)

$p>0.05$ in all comparisons. T1 = Immediate-30minute, T2 = 30-minute to 1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

TLE6

TLE6 was matched with 7 healthy controls (5 females, 2 males) who were matched for age ($t(6) = 0.067$, $p=0.949$, IQ ($t(6) = 0.079$, $p=0.940$) years in education ($t(6) = 0.766$, $p=0.473$), anxiety ($t(6) = -0.921$, $p=0.393$) and depression ($t(6) = 0.701$, $p=0.510$). Initial learning was adequately matched on all tests.

Examination of scores on the AMPIB indicates that her memory for verbal and visual material over short delays is intact. On visual experimental tests, ALF was evidenced on spatial recall ($t(6) = 2.169$, $p=0.037$). On verbal experimental tests, ALF was demonstrated by recall ($t(6) = 5.867$, $p=0.001$) and recognition ($t(6) = 4.382$, $p=0.002$) of the 'long-delay story.'

Table 9: Forgetting scores of TLE6 and control sub-group on assessments of ALF

	TLE6	Control Mean (SD)
N	1	7
Visual Tests		
Item Recall T1	-1	2.43 (4.39)
Item Recall T2	8	6.14 (3.80)
Spatial Recall (*s*) T1	-0.21	0.65 (1.18)
Spatial Recall (*s*) T2	4.06	1.82 (0.97)*
Descriptive Recall (*d)* T1	4.25	12.91 (14.43)
Descriptive Recall (*d*) T2	22.22	5.90 (19.35)
Recognition Sensitivity (*d'*) T1	0.39	0.35 (0.80)
Recognition Sensitivity (*d'*) T2	0.96	1.59 (0.61)
Verbal Stories		
Short-Delay Story Recall	3	1.29 (1.11)
Short-Delay Story Recognition	0	-0.14 (0.38)
Long-Delay Story Recall	14	2.71 (1.80)**
Long-Delay Story Recognition	6	1.43 (0.98)**
Repeated Story Recall T1	5	1.29 (1.98)
Repeated Story Recognition T1	1	0.71 (0.76)
Repeated Story Recall T2	10	2.14 (4.06)
Repeated Story Recognition T2	5	0.00 (1.00)

*p<0.05, **p<0.01 T1 = Immediate-30minute, T2 = 30-minute-1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

Results indicate that recall and recognition of verbal and visual material over short delays is intact. Regarding visual information, only forgetting of spatial locations is accelerated thereafter. Her forgetting of verbal information was also accelerated over the long delay; however since her memory for the repeated story was entirely intact, there is a possibility that repeated recall may attenuate the affects ALF.

TLE7

TLE7 was matched with 6 healthy controls (1 female, 5 males) who were matched for age (t(5) = -0.180, p=0.864), years in education (t(5) = -1.148, p=0.303), anxiety (t(5) = -1.395, p=0.222) and depression (t(5) = 1.056, p=0.339). It was not possible to match for IQ (t(5) = -3.648, p=0.015) with controls being significantly higher (range = 98-114). Initial learning was equated on all verbal tests, however there were significant differences on item recall (t(5) = -3.320, p=0.011), spatial recall (t(5) =-3.706, p=0.007), descriptive recall (t(5) =-5.123, p=0.002) and recognition (t(5) =-3.305, p=0.011).

Table 10: Forgetting scores of TLE7 and control sub-group on assessments of ALF

	TLE7	Control Mean (SD)
N	1	6
Visual Tests		
Item Recall T1	3	0.50 (0.55) **
Item Recall T2	5	4.67 (3.20)
Spatial Recall (*s*) T1	0.89	0.11 (0.12) ***
Spatial Recall (*s*) T2	3.77	1.18 (0.84) *
Descriptive Recall (*d)* T1	-17.14	-3.97 (11.29)
Descriptive Recall (*d*) T2	7.14	16.97 (9.47)
Recognition Sensitivity (*d'*) T1	-0.65	0.35 (0.56)
Recognition Sensitivity (*d'*) T2	1.45	1.52 (0.82)
Verbal Stories		
Short-Delay Story Recall	3	0.50 (1.76)
Short-Delay Story Recognition	-2	0.17 (0.75)
Long-Delay Story Recall	12	5.50 (1.38) **
Long-Delay Story Recognition	5	2.0 (1.67)
Repeated Story Recall T1	2	1.67 (4.72)
Repeated Story Recognition T1	0	0.33 (0.52)
Repeated Story Recall T2	2	2.50 (2.81)
Repeated Story Recognition T2	1	0.17 (1.17)

* $p<0.05$, ** $p<0.01$, *** $p\leq0.001$ T1 = Immediate-30minute, T2 = 30-minute-1-week. Recognition sensitivity scores represent the difference in sensitivity between delays.

Examination of scores on the BMIPB indicates his memory for verbal and visual material over short delays is below average. On visual experimental tests, forgetting was found to be accelerated over the long delay on spatial recall ($t(5) = 2.856$, $p=0.018$). Forgetting was also found to be significantly accelerated over the short delay for item recall ($t(5) =4.226$, $p=0.004$) and spatial recall ($t(5) = 5.906$, $p=0.001$). On verbal experimental tests ALF was demonstrated by recall of the 'long-delay story' ($t(5) = 4.366$, $p=0.004$).

Results indicate that forgetting was already accelerated for visual information over the short delay. Forgetting of verbal information as assessed by recall is accelerated over longer delays; however repeated recall may be sufficient to attenuate this.

Individual Analysis

Forgetting rates (as calculated by subtracting scores at one week from scores on immediate tests) were analysed on an individual basis to examine the prevalence of ALF within both groups. The percentage of TLE and control participants showing impaired retention (i.e. forgetting greater than 1.96 standard deviations from the mean of the controls) after one week can be seen in Figure 10.

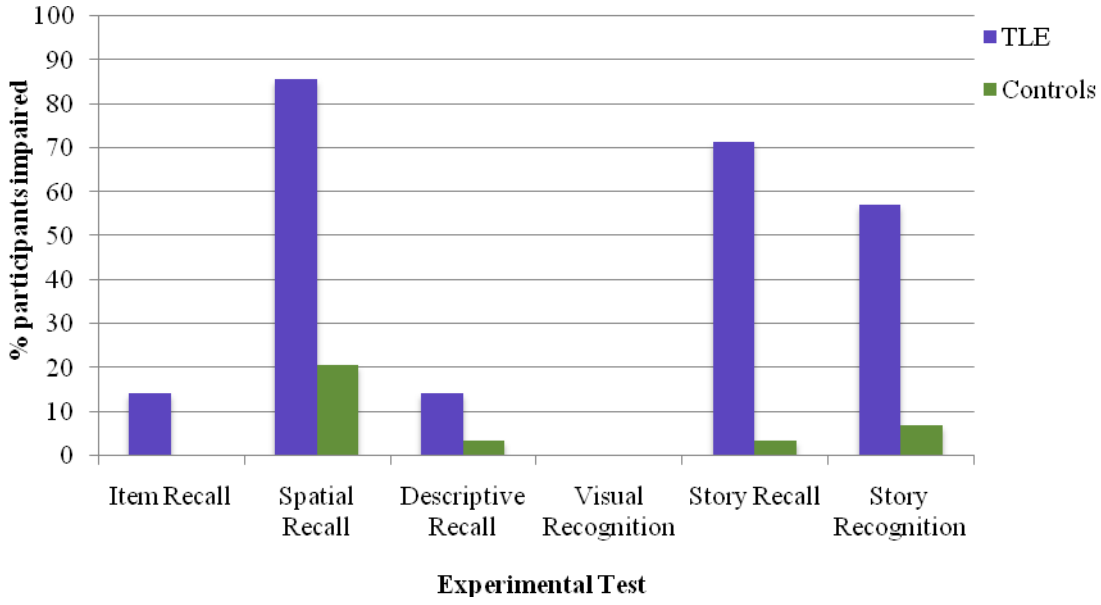


Figure 10. Percentage of TLE and control participants impaired at the long-delay on each experimental test.

DISCUSSION

The results will now be discussed in relation to each hypothesis and consideration will be given to the study's original aims.

Test Development

In line with the original aims, this study has provided a repeatable battery of tests to assess verbal and visual forgetting over long delays. The large number of photographs within the visual scenes test is likely to minimise the potential for rehearsal however a noteworthy limitation is the lengthy administration time, particularly when the multiple presentation procedure is required to equate initial learning. A limitation of the verbal tests is that they can only assess forgetting of semantically related material. Although Butler & Zeman (2008) suggested useful comparisons could be drawn by also employing unrelated material (e.g. a word list), it is argued here that stories are more ecologically valid and clinically useful. However, given that normal rates of forgetting are thought to differ with psychological variables such as meaningfulness of the material (Lezak, 2004 pg. 30) it is still possible that forgetting of everyday events may differ due to their personal saliency.

Is forgetting accelerated in people with TLE?

Using these new stimuli, forgetting of stories and visual scenes in people with TLE and healthy controls was assessed using recall and recognition tests at the standard 30-minute delay and following a long-delay of one week. Previous case studies of ALF have been complicated by factors in addition to TLE such as damage resulting from closed head injury (Mayes et al., 2003). Previous group studies of ALF in TLE have reported mixed results; some have found evidence for ALF (Blake et al., 2000; Butler et al., 2007; Manes et al., 2005; Mameniskiene et al., 2005; Martin et al., 1991) and others

have not (Bell et al., 2005; Bell, 2006; Giovagnoli et al., 1995). These discrepancies have been attributed to methodological confounds such as inadequate matching of intellectual ability and initial learning, floor effects (Butler & Zeman, 2008) and overlearning and related ceiling effects (Bell et al., 2005).

In an attempt to protect against methodological confounds, this study utilised a multiple-presentation procedure to equate initial learning whilst avoiding overlearning associated with learning to criterion. To avoid floor and ceiling effects as far as possible experimental material was systematically piloted. At a group level this was successful with initial learning equated between groups and no evidence of floor and ceiling effects within group means. Individual analysis indicated variability however and was successful in four cases (TLE1, TLE2, TLE5 and TLE6). Of these, evidence of ALF was demonstrated by three participants (TLE1, TLE2 and TLE6) on some tests. As has been the case in previous studies, analyses of forgetting on tests where confounds were not effectively avoided may not be reliable.

Matching for IQ was an additional problem as no control participants were recruited with an IQ below 95. Years in education were matched in all cases but this would not generally be considered satisfactory when drawing comparisons with a neurologically impaired group. Although IQ was not found to exert a significant effect on forgetting, caution must still be applied to interpretation of results where IQ was not adequately matched due to widely accepted association between low IQ and poor memory (Mayes, 1986) and the possibility that lower IQ will be associated with faster forgetting. This issue applies to the group analysis and individual analysis of TLE4, TLE2, TLE5 and TLE7.

There were two participants (TLE1 and TLE6) for whom all the described methodological confounds were avoided and evidence of ALF was still found. This indicates that methodology cannot account for all the dissociations observed, providing evidence to support the hypothesis that people with TLE can experience genuine ALF. This is contrary to the view of Bell et al. (2006) who proposed that overlearning could account for the effects observed in studies reporting ALF. However, interpretation is not straightforward as individual analysis uncovered healthy participants who showed ALF for verbal and visual information on experimental tests. Although the prevalence of ALF was higher within the TLE group, this finding throws into question the supposed direct association between ALF and TLE. Furthermore, the results of this study indicate that the existence of ALF in TLE may not be 'typical.'

Visual Scenes Recall & Recognition

Group analysis revealed that item recall was comparable between groups, however forgetting of spatial and descriptive information was accelerated in the TLE group over the long delay. Case-series analysis uncovered mixed results. There were no significant differences in forgetting of visual information for two participants (TLE4, TLE3); however examination of raw scores revealed these participants were unable to recall any information at the long-delay. Therefore, in both cases the presence of floor effects and poor initial learning may have caused forgetting rates to be underestimated. For one participant (TLE7) forgetting was already accelerated over 30-minutes as measured by recall of item and spatial information. One participant (TLE2) demonstrated accelerated forgetting for item and descriptive information and two participants (TLE6 and TLE1) demonstrated accelerated forgetting of spatial information over long-delays. The final participant (TLE5) showed comparable rates of forgetting to controls on all visual experimental tests. Overall, results suggest that

people with TLE may be vulnerable to accelerated forgetting of visual information; however there is considerable individual variation.

No significant differences in visual scene recognition sensitivity or bias were found in the group or case-series analysis. This suggests that visual recognition memory is not affected by ALF and therefore recognition may be intact after long delays even when recall is impaired. This suggests that only the information important for recall (not recognition) is lost from memory. It is difficult to comment on how well this result generalises to existing literature as previous studies of ALF have failed to routinely assess visual recognition memory over longer delays. The only group study to do so (Manes et al, 2005) found no evidence of accelerated forgetting which supports our findings.

Story Recall & Recognition

Group analysis of target stories revealed that long-term forgetting was accelerated in the TLE group, affecting both recall and recognition. However, there was evidence to suggest that forgetting was already accelerated over 30-minutes (but only on recall, not recognition). As Bell et al. (2005) and Bell (2006) argued, this suggests that testing at the standard delay may be sufficient to identify accelerated forgetting in TLE participants.

Again, results from case-series analysis were mixed, highlighting the considerable individual variability. The performance of one participant (TLE5) was entirely intact on all verbal experimental tests. One participant (TLE4) demonstrated accelerated forgetting over the short delay and then performance declined to floor level at the end of the long-delay. For TLE3, it was not possible to draw any reliable conclusions due

differences in initial learning and floor and ceiling effects. However, (although the contribution of lower IQ cannot be entirely ruled out in the cases of TLE2 and TLE7), four participants (TLE1, TLE2, TLE6 and TLE7), demonstrated robust evidence of ALF with their recall of the target stories being comparable to controls up to 30-minutes followed by accelerated forgetting thereafter.

In three cases, ALF also affected verbal recognition performance (TLE1, TLE2, and TLE6). This indicates that verbal recognition memory may be vulnerable to accelerated forgetting in addition to verbal recall. This supports the hypothesis that even in the face of intact initial encoding and normal performance at 30-minutes; memories remain vulnerable and can be disrupted during an extended period of consolidation required for the long-term maintenance of memories.

Does laterality of seizure onset result in a material-specific deficit?

This study assessed forgetting of verbal and visual material over long-delays. Laterality of seizure focus was confirmed by EEG and in all cases this was consistent with MRI evidence of structural lesions. This enabled examination of whether participants affected by ALF demonstrated the expected material-specific deficits. With specific regard to ALF, existing evidence is both limited and inconclusive (Butler & Zeman, 2008). Drawing upon more general literature considering memory deficits in TLE (e.g. Hermann et al., 1997), it may be expected that participants with right-sided seizure onset would show ALF for visual scenes and participants with left-sided TLE would show ALF for verbal material. Given the small TLE sample size, it was not considered meaningful to compute comparisons between groups of left-sided and right-sided seizure onset. In relation to this hypothesis, consideration is therefore given solely to data from case-series analysis.

None of the four TLE participants with right-sided seizure onset demonstrated material-specific ALF for visual material. One participant (TLE5) was not impaired on any measures, one participant (TLE4) performed at floor levels on a range of verbal and visual tests at the long delay and two participants (TLE6 & TLE7) were also impaired on story recall. Similarly, none of the three participants with left-sided seizure onset demonstrated material-specific ALF for verbal material. Although TLE1 was predominantly impaired on verbal tests, he also showed accelerated forgetting for spatial information. TLE2 evidenced accelerated forgetting for both verbal and visual material and TLE3 performed at floor level on a range or verbal and visual tests at the long delay.

Contrary to the original hypotheses, these findings indicate that patterns of forgetting are not generally related to laterality of seizure focus. This is not consistent with the material-specific memory model which presumes that damage to the left temporal lobe is associated with impairments in verbal memory (e.g. Milner, 1970) and damage to the right temporal lobe is associated with impaired visuo-spatial memory (e.g. Delaney et al., 1980). Instead, the current findings are aligned with a recent review paper proposing that verbal and non-verbal memory functions are not entirely lateralised in mesial TLE (Saling, 2009). For example, the variable results found within participants with right-sided TLE may relate to the findings of a functional MRI study conducted by Dupont et al., (2002) which indicated that there can be a bilateral hemispheric alteration of memory processes in right medial TLE. An additional reason why participants with left-sided seizure onset also demonstrated ALF for visuo-spatial information may be due to the visual scenes test having a strong verbal component. This gives rise to the possibility that visuo-spatial information was encoded both non-verbally and verbally. An alternative possibility is that the development of TLE in childhood allows for

functional reorganisation and the resultant expectancy that people may not show strong hemispheric specialisation (e.g. Jokeit et al., 1996).

Does repeated recall and rehearsal attenuate ALF?

A novel story recall paradigm was devised to reduce rehearsal for target stories whilst providing the opportunity to assess the effects of repeated testing. Having been instructed to concentrate more specifically on the repeated story, it is also likely that this story benefited from increased attention and rehearsal.

Group analysis of the repeated story evidenced that recall was intact in both groups at 30-minutes and there was a trend towards the TLE group showing faster forgetting over the long delay. This is contrary to forgetting of the target stories which were clearly accelerated over both the short and long delay. Case-series analysis revealed that out of the four participants who demonstrated ALF for the 'long-delay story', three (TLE1, TLE6, TLE7) showed comparable forgetting rates to controls for the repeated story. This (albeit tenuously) suggests that repeated recall and specific instructions to focus attention have the potential to attenuate the effects of ALF. This finding supports Jansari et al. (in press) who reported data from participant RY which indicated that performance was normal if verbal stories were repeatedly recalled, yet significantly impaired within 24 hours in the absence of repeated recall. Future studies may wish to consider evaluating the robustness of these findings as they may have important clinical implications in informing compensatory or restorative strategies.

Is accelerated forgetting related to epileptiform activity?

Group comparisons (seizure, seizure-free) indicated that experiencing seizures during the delay did not significantly affect retention. This result is in line with the findings of

Blake et al. (2000); however the very small sample sizes reduce the reliability and generalisability of this conclusion. Given that other studies report opposing results (e.g. Mameniskiene et al., 2006), further exploration is clearly warranted. An additional avenue for consideration is the potential role of subclinical seizures. It is also possible that people with TLE have a poor overall memory as a result of enduring TLE for many years and/or experiencing a high seizure frequency.

CONCLUSIONS

As is now widely accepted, ALF is most convincingly demonstrated when initial learning and 30-minute recall and recognition is normal but rapid forgetting is observed over longer delays (Butler & Zeman, 2008). Regarding the existence of ALF in people with TLE, this study has found mixed results. Despite the application of more robust methodology, it has been difficult to draw definitive conclusions. This reflects the considerable individual variation found in the forgetting profiles of participants with TLE. This study has evidenced that even when assessed using the same battery of tests, it is possible to find some people who show clear ALF, some are already impaired at the standard 30-minute delay and some whose memory is intact. Although conducting group and case-series analysis allowed for more comprehensive examination of ALF, it is acknowledged that results from the group analysis must be treated with caution due to the small TLE sample reducing the power of analysis and variability. Furthermore, in the absence of well-powered group analysis, the potential of anticonvulsant medication, duration of epilepsy or frequency of seizures exerting a specific effect on forgetting cannot be ruled out.

The presence of accelerated forgetting observed in the group analysis supports the findings of Blake et al. (2000); the first study to report ALF in pre-surgical TLE

participants. The findings of Blake et al are also extended by evidence that ALF can be observed in pre-surgical TLE participants for non-verbal material in addition to verbal material. Our mixed findings at an individual level are supportive of Bell et al. (2005) who stressed that accelerated forgetting is uncommon in people with TLE.

Interestingly, this study found that control participants can also show very poor retention over long-delays. As suggested by MacDonald et al., (2006), this raises the possibility of there being considerable variation in forgetting amongst the healthy population. Whilst the claim of Bell (2006) that more controls than TLE participants show increased forgetting at an individual level was not supported, the possibility that ALF is prevalent within the normal population clearly warrants further investigation.

Theoretical Implications

This study has evidenced that people with TLE can exhibit normal learning and normal performance after a short delay yet show accelerated forgetting thereafter. As Blake et al. (2000) acknowledged this is robust evidence that memories can remain vulnerable beyond the standard 30-minute delay and fits well with the extended period of consolidation proposed by Squire et al., (1995) which has been adopted by previous studies to account for ALF (Blake et al., 2000; Kapur et al., 1997). The reason why participants with TLE presented with varying degrees of vulnerability to disruption to the consolidation process remains unclear. As such, the question as to whether ALF reflects a mild form of amnesia or a separate forgetting phenomenon remains unanswered. Theoretically, the failure to find a deficit in visual recognition memory also means that the possibility of ALF being related to deficient memory retrieval cannot be ruled out either.

Clinical Implications

These findings suggest that whilst some people with temporal lobe epilepsy will demonstrate memory loss within the 30-minute time period of standardized assessments, there is a subset of people who exhibit memory impairments which may be missed by routine neuropsychological assessments. This (albeit possibly infrequent) existence of ALF in the absence of methodological confounds raises questions about the utility of existing standardised tests to assess memory in this population. In future, test developers may therefore want to consider acquiring normative data for a long-delay trial when developing or revising standardised tests. To avoid unnecessarily wasting clinic time, the recommendation would be to begin with standard assessment procedures but maintain vigilance for individuals who perform normally on these tests, yet report everyday memory problems. In these cases, assessment beyond the usual 30-minute retention period may be required to obtain a complete picture of an individual's memory impairments.

The considerable individual variation between TLE participants further highlights the importance of individually tailored assessments in clarifying patterns of impairment to inform future management plans. For people where an extended consolidation deficit is indentified, these results would suggest that repeatedly recalling and rehearsing new information may protect against abnormal forgetting by reinforcing consolidation. On an everyday practical basis, this could involve engaging friends and relatives in conversations about recent events.

Future Directions

The TLE participants in this study were all being considered for epilepsy surgery. This affords the possibility of conducting re-assessments using the repeatable tests which

have been developed. Studying the effects of surgery on ALF will allow for further investigation of how structural damage in the temporal lobe and seizure activity may be disrupting memory storage.

Given the heterogeneous nature of this group and the individual idiosyncrasies highlighted by this study, it would be advisable for future studies to continue to combine group and individual analysis. Furthermore, it cannot be presumed that ALF is a phenomenon limited to TLE and the possibility that ALF may be present in healthy individuals and in other neurological conditions reflecting a different underlying pathology warrants further investigation.

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APPENDIX A

FORMATS

1. Letter Approving Journal Selection
2. Copies of current guidelines for authors for specified journals

    2.1 Clinical Psychology Review (Literature Review)

    *** Removed from eThesis to conform with copyright legislation*

    2.2 Epilepsia (Research Report)

    *** Removed from eThesis to conform with copyright legislation*

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Doctor of Clinical Psychology (DClin Psy) Programme
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9 February 2010

Gemma Elliott
Third year trainee
Clinical Psychology Unit
University of Sheffield

Dear Gemma

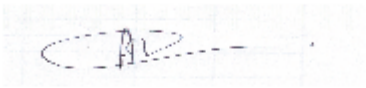
I am writing to indicate our approval of the journal(s) you have nominated for publishing work contained in your research thesis.

Literature Review: Clinical Psychology Review

Research Report: Epilepsia

Please ensure that you bind this letter and copies of the relevant Instructions to Authors into an appendix in your thesis.

Yours sincerely



Dr Andrew Thompson
Director of Research Training

APPENDIX B

ETHICAL APPROVAL

1. Copy of Approval Letter from South Yorkshire Ethics Committee

National Research Ethics Service
South Yorkshire Research Ethics Committee
1st Floor Vickers Corridor
Northern General Hospital
Herries Road
Sheffield
S5 7AU

Telephone: 0114 226 9153
Facsimile: 0114 256 2469
Email: joan.brown@sth.nhs.uk

18 June 2009

Miss Gemma L Elliott
Clinical Psychology Unit
The University of Sheffield
Western Bank
Sheffield
S10 2TN

Dear Miss Elliott

Study Title:	**Is forgetting accelerated in patients with temporal lobe epilepsy? A study pre and post-surgery.**
REC reference number:	**09/H1310/45**
Protocol number:	**3**

Thank you for your letter of 12 June 2009, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk
Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Email Recruitment Advertisement1	1	05 May 2009
Recruitment - Reply Slip	1	05 May 2009
Recruitment Poster - Control Group	1	05 May 2009
Scientific Review Correspondence		
Supervisor's CV - Claire Isaac		
Covering Letter		10 May 2009
Investigator CV		10 May 2009
Application		10 May 2009
Covering letter addressing points raised by committee in provisional opinion letter		12 June 2009
Response to Request for Further Information		12 June 2009
Participant Consent Form	1	12 June 2009
Participant Consent Form	3	12 June 2009
Participant Information Sheet: Healthy Volunteers	1	12 June 2009
Participant Information Sheet	2	12 June 2009
Protocol	3	12 June 2009

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

09/H1310/45	**Please quote this number on all correspondence**

Yours sincerely

J Brew

Jo Abbott
Chair

Enclosures: **"After ethical review – guidance for researchers" SL-AR2**

Copy to: **STH R&D Department**

APPENDIX C

MEASURES

1. Wechsler Test of Adult Reading (WTAR) *** Removed from eThesis to conform with copyright legislation*
2. Visual Scenes Tests
    - 2.1. Recall Scenes (set A and set B)
    - 2.2. Exemplar Recall Response Form
    - 2.3. Spatial Recall Response Grid
    - 2.4. Exemplar Visual Recognition Scenes
    - 2.5. Exemplar Recognition Response Form
3. Verbal Stories Tests
    - 3.1. Stories (set A and set B)
    - 3.2. Exemplar Story Recall Response Form
    - 3.3. Exemplar Story Recognition Response Form
4. Long-Term Memory Questionnaire
5. Hospital Anxiety and Depression Scale (HADS) *** Removed from eThesis to conform with copyright legislation*
6. Seizure Diary

1. Wechsler Test of Adult Reading (WTAR)

*** Removed from eThesis to conform with copyright legislation*

2. Visual Scenes Tests

*2.1: **Recall** - Set A*

NB: Actual size of scenes during initial presentation was 12” x 9” to fill PC Laptop Screen

A1: The Bakery Scene

A2: The Office Scene

A3: The River Scene

A4: The Bar Scene

A5: The Bathroom Scene

A6: The Stables Scene

A7: The Supermarket Scene

A8: The Winter Scene

A9: The Kitchen Scene

2.1: Recall *- Set B*

B1: The Park Scene

B2: The Flat Scene

B3: The Classroom Scene

B4: The Car Boot Scene

B5: The Camping Scene

B6: The Playroom Scene

B7: The Garden Scene

B8: The Beach Scene

B9: The Library Scene

2.2. *Exemplar Recall Response Form:* A1 'The Bakery Scene'

ITEM RECALL: Can you tell me what was in The Bakery Scene?

- □ Baker / lady
- □ Girl
- □ Cabinet / cake display
- □ Drink
- □ Windows
- □ Clock
- □ Bag
- □ Gingerbread man

Other:_____ Score 0 – 6:_____

SPATIAL RECALL: Can you tell me where [insert item recalled] was? *(show participant the recall grid)*

- □ Baker / lady: 2
- □ Girl: 1 / 3
- □ Cabinet / display of cakes: 3 / 4
- □ Drink: 2
- □ Windows: 1 / 2
- □ Clock: 2
- □ Bag: 3
- □ Gingerbread man: 4

Other:_____ Score 0 – 6:_____

DESCRIPTIVE RECALL: Can you tell me what it / they looked like / what they were doing? *(Record descriptions of up to 2 attributes for up to 6 items previously recalled)*

☐ ☐ **Baker / lady** (e.g. serving the girl / passing the girl a drink*, old/,middle aged, wearing glasses, [blue] apron, [white] shirt, broach, gold earrings, short hair, ginger/blond hair, smiling)

☐ ☐ **Girl** (e.g. young, brown hair, [plaited] pigtails, [green] vest-top, [beige/cream] shorts, taking a drink from the lady*, smiling, carrying a bag*)

☐ ☐ **Cabinet / display of cakes** (3-4 shelves, many different types, pastries, gingerbread man*, buns on top shelf have cherries on, clear plastic/glass display)

☐ ☐ **Drink** (cola/coke, straw, in a glass, being passed between young girl and lady*)

☐ ☐ **Windows** (red tie-backs, brown wooden frames, 4 visible, wooden bars in a cross pattern, net curtains, white/cream net curtains, curtains hanging at top and bottom)

☐ ☐ **Clock** (round, dark brown outer frame, silver/chrome inner face, no numbers, [silver] roman numeral markers, time shows ten past ten, second hand at 12)

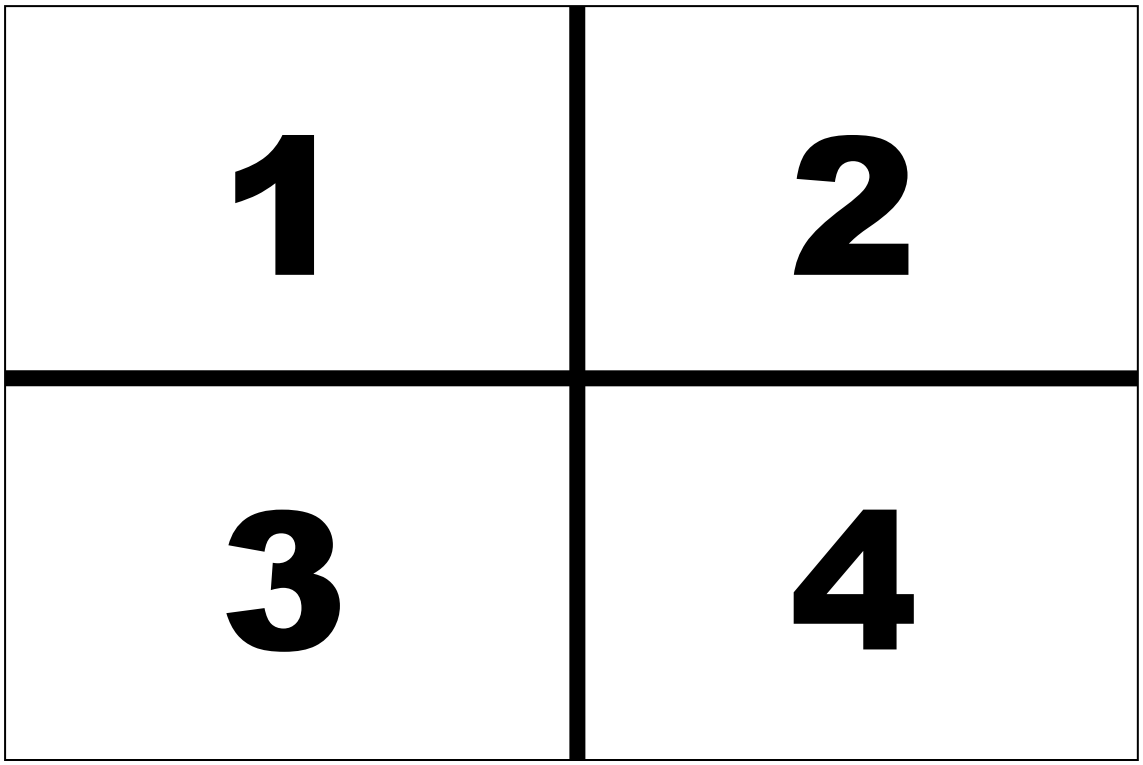
☐ ☐ **Bag** (carried by the girl*, carried in right hand, blue, pink flowers/ roses/green leaves, rectangle shape

☐ ☐ **Gingerbread man*** (in the cabinet / on the shelf, Santa Claus hat / red hat, white piping / icing, smiling, flower buttons)

** Only one point can be awarded for each description. The description may be scored for any of the items it relates to.*

Score 0 – 12:

2.3. Spatial Recall Response Grid



NB: Actual grid size during testing was A4

2.4. Exemplar Visual Recognition Scenes

NB: Actual size of scenes during initial presentation & recognition testing was 12” x 9” to fill PC Laptop Screen

Set A: Example of Recognition Target

Set B: Example of Recognition Target

2.5. Exemplar Visual Recognition Response Form: Set A, Test 1

Participant No_____ **Delay:** ☐ Immediate ☐ 30 minute ☐ 1 week

Slide number	Response (Y / N)	Correct Response	Score
1	***Instructions***	***Instructions***	-
2		**Y**	
3		**N**	
4		**N**	
5		**Y**	
6		**Y**	
7		**Y**	
8		**N**	
9		**N**	
10		**N**	
11		**Y**	
12		**Y**	
13		**N**	
14		**N**	
15		**Y**	
16		**Y**	
17		**N**	
18		**Y**	
19		**N**	
20		**N**	
21		**Y**	
22		**Y**	
23		**N**	
24		**N**	
25		**Y**	
26		**Y**	
27		**Y**	
28		**N**	
29		**N**	
30		**N**	
31		**Y**	
32		**N**	
33		**Y**	
34		**Y**	
35		**N**	
36		**Y**	
37		**N**	
38		**N**	
39		**N**	
40		**Y**	
41		**Y**	
42		**Y**	
43		**N**	
44		**Y**	
45		**N**	
46		**Y**	
47		**Y**	
48		**Y**	
49		**N**	
50		**N**	
51		**N**	

Slide number	Response (Y / N)	Correct Response	Score
52		**Y**	
53		**Y**	
54		**N**	
55		**N**	
56		**N**	
57		**Y**	
58		**N**	
59		**Y**	
60		**N**	
61		**Y**	
62		**Y**	
63		**N**	
64		**N**	
65		**Y**	
66		**N**	
67		**N**	
68		**Y**	
69		**Y**	
70		**Y**	
71		**N**	
72		**Y**	
73		**N**	
74		**N**	
75		**Y**	
76		**N**	
77		**Y**	
78		**Y**	
79		**N**	
80		**Y**	
81		**N**	
82		**N**	
83		**Y**	
84		**Y**	
85		**N**	
86		**Y**	
87		**N**	
88		**N**	
89		**N**	
90		**Y**	
91		**Y**	
92		**Y**	
93		**N**	
94		**Y**	
95		**N**	
96		**N**	
97		**Y**	
98		**N**	
99		**Y**	
100		**Y**	
101		**N**	
Total Correct (max 100)			

3. Verbal Stories Tests

3.1. Stories (set A and set B)

Set A

1. On the 12th April, Peter Brooks from Gloucester becomes the first man to travel around the coast of Britain in a wheel-chair. The 27 year old lost the use of his legs six years ago in a car accident. The 4000 mile trip took 14 weeks and raised 50,000 pounds for facilities for the disabled in Cheltenham.

2. Pensioner, Tom Williams was strolling down Apple Grove when he noticed smoke pouring from the downstairs window of a nearby house. Despite having suffered from a heart attack only six months before, he dashed to the rear of the blazing house, forced open the lounge doors and dragged out the unconscious occupant.

3. Eighty year old Bob Ward from Kent has lived in a council flat since he retired 15 years ago. Last Friday, a letter arrived announcing that he had won 85,000 pounds on a premium bond. This had belonged to his wife Mary who died ten years ago. He now plans to move near his daughter.

Set B

1. Eleven year old Warren Massingham from the Midlands was frequently terrorised on the playing field of the large comprehensive school which he attended. On the 14th July 1974, his grandparents sent him on an adventure holiday where he spent six weeks doing activities like rock climbing and abseiling. On returning to school, his newly acquired self-confidence soon caused the bullying to stop.

2. Unemployed factory worker, George Powell was returning from a club in Birmingham on Monday night at 3am when he found the body of an elderly man slumped against a wall in Queen Street. He had been badly beaten up and blood was still welling from a deep cut on his temple. George quickly phoned an ambulance which took the victim to the local infirmary.

3. A holidaymaker in Italy almost drowned on 27th May after being severely stung by a Portuguese-man-of-war. 32 year old Richard White from Canterbury was about 100 yards from the shore in Rimini when he swam into the jellyfish. Despite being stung over 250 times he attracted the attention of a yacht owner, who picked him up. Authorities have warned tourists of the danger.

*3.2. **Exemplar Story Recall Response Form:** Set A, Story 1*

Participant No_____

Story 1

Delay: □ Immediate □ 30 minute □ 1 week Prompt given □

On the 12th/ April, /Peter /Brooks /from Gloucester /became the first man/ to travel around the coast /of Britain /in a wheel-chair. /The 27 year old/ lost the use of his legs /six years ago /in a car /accident. /The 4000 mile trip /took 14 weeks / and raised 50 000 pounds/ for facilities /for the disabled / in Cheltenham.

Total score (max 20):_____

Delay: □ Immediate □ 30 minute □ 1 week Prompt given □

On the 12th/ April, /Peter /Brooks /from Gloucester /became the first man/ to travel around the coast/ of Britain /in a wheel-chair. /The 27 year old/ lost the use of his legs /six years ago /in a car /accident. /The 4000 mile trip /took 14 weeks / and raised 50 000 pounds/ for facilities /for the disabled / in Cheltenham.

Total score (max 20):_____

Delay: □ Immediate □ 30 minute □ 1 week Prompt given □

On the 12th/ April, /Peter /Brooks /from Gloucester /became the first man /to travel around the coast /of Britain /in a wheel-chair. /The 27 year old/ lost the use of his legs /six years ago/ in a car /accident. /The 4000 mile trip /took 14 weeks / and raised 50 000 pounds/ for facilities /for the disabled/ in Cheltenham.

3.3. Exemplar Story Recognition Response Form: Set A, Story 1

Participant No_____ **Delay Key:** ☐ Immediate ◊ 30 minute ◯ 1 week

Story 1: *Tick the box next to the answer given (correct responses shown in bold)*

1. What was the man's name?
   - ☐ ◊ ○ **Peter Brooks**
   - ☐ ◊ ○ Peter Butcher
   - ☐ ◊ ○ Paul Brocks
   - ☐ ◊ ○ Paul Bailey
2. Where was he from?
   - ☐ ◊ ○ Cheltenham
   - ☐ ◊ ○ Worcester
   - ☐ ◊ ○ **Gloucester**
   - ☐ ◊ ○ Salisbury
3. Where did he travel?
   - ☐ ◊ ○ Around the coast of France
   - ☐ ◊ ○ Around the coast of Ireland
   - ☐ ◊ ○ **Around the coast of Britain**
   - ☐ ◊ ○ Across Britain
4. How did he travel?
   - ☐ ◊ ○ By bicycle
   - ☐ ◊ ○ **In a wheel-chair**
   - ☐ ◊ ○ On foot
   - ☐ ◊ ○ On crutches
5. When did he complete his journey?
   - ☐ ◊ ○ 21st August
   - ☐ ◊ ○ **12th April**
   - ☐ ◊ ○ 12th August
   - ☐ ◊ ○ 21st April
6. How old was he?
   - ☐ ◊ ○ 25
   - ☐ ◊ ○ 29
   - ☐ ◊ ○ **27**
   - ☐ ◊ ○ 23

7. What happened six years ago?

- ☐ ◊ ○ **He was involved in a car accident**
- ☐ ◊ ○ He was involved in a motor-cycle accident
- ☐ ◊ ○ He fell off a roof
- ☐ ◊ ○ He fell off a ladder

8. How many miles was the trip?

- ☐ ◊ ○ 2000
- ☐ ◊ ○ 5000
- ☐ ◊ ○ 3000
- ☐ ◊ ○ **4000**

9. How long did the trip take?

- ☐ ◊ ○ 4 weeks
- ☐ ◊ ○ **14 weeks**
- ☐ ◊ ○ 4 months
- ☐ ◊ ○ 40 days

10. How much money did he raise?

- ☐ ◊ ○ 100 000 pounds
- ☐ ◊ ○ 10 000 pounds
- ☐ ◊ ○ 5000 pounds
- ☐ ◊ ○ **50 000 pounds**

11. What was the money to be used for?

- ☐ ◊ ○ A spinal injuries unit
- ☐ ◊ ○ A children's hospital
- ☐ ◊ ○ **Facilities for the disabled**
- ☐ ◊ ○ The disabled Olympics

12. Where was the money to be used?

- ☐ ◊ ○ **Cheltenham**
- ☐ ◊ ○ Salisbury
- ☐ ◊ ○ Worcester
- ☐ ◊ ○ Gloucester

Score (max 12):_____

4. Long-Term Memory Questionnaire

MEMORY QUESTIONNAIRE

In this questionnaire we would like you to think about the way your memory has been working.

PERSONAL DETAILS Participant ID _____

DATE OF BIRTH _____

FIRST LANGUAGE _____

GENDER Male Female (please circle)

If someone is helping you fill in this questionnaire, please tell us who this is:

_____

General Questions

When did your epilepsy start? _____

Details of last seizure (date, time and type if known)

_____

_____

_____

Do you have problems with your memory? Yes/No (circle one)

If Yes, please answer the following questions:

Do you forget things more quickly than you used to? Yes/No (circle one)

If yes, does this forgetting occur (please tick as appropriate):

in the first few minutes _____

in the first few hours _____

over a number of days _____

over a number of weeks _____

other (describe) _____

5. Hospital Anxiety and Depression Scale (HADS)

*** Removed from eThesis to conform with copyright legislation*

6. SEIZURE DIARY

If you experience any seizures during the next week, please give details below. We would like you to record when the seizure occurred (day and time) and the type of seizure (if known).

Date	**Time**	**Type of seizure** (e.g. generalised, tonic-clonic, absences or auras, simple partial, complex partial).

APPENDIX D

TEST DEVELOPMENT

1. Piloting verbal and visual material to evaluate forgetting over long-delays
2. Matching final sets for difficulty

1. PILOT PHASE

Participants

8 healthy participants (6 female, 2 male) took part in the piloting of verbal and visual materials to evaluate forgetting over long delays. Their mean age was 28.87 years (SD = 3.68, range 24-32).

Method

Pilot participants completed either set A or B in two sessions spaced a week apart. The first session was used to present the stimuli and test immediate and 30-minute recall and recognition. The second session assessed participants' memory for the material following a week delay. The aim was to ensure all stimuli could be successfully recalled or recognised by healthy participants over the three delays without evidence of floor or ceiling effects. If such effects were observed, experimental manipulations were made in effort to avoid these confounds. After three participants had completed either set A or set B, performance was reviewed, qualitative comments and observations were considered and amendments were made if necessary.

Initial Test Materials & Procedure

Upon commencement of piloting, two matched sets of tests to assess forgetting over long-delays had been created (set A and set B). Each set contained a visual scenes test and a verbal stories test, each of which included three parallel tests of recall and recognition. This afforded the possibility of testing memory immediately, after a short delay of 30-minutes and after a long-delay of 1 week.

Each visual scenes test comprised of 150 recognition targets, 150 recognition foils and 12 recall scenes. Each recall scene and recognition target appeared once during the

initial presentation for 5 seconds and 2 seconds respectively during which time participants had to name something in each picture. Memory for three of the recall scenes was tested at each delay, with participants being required to recall the items in the scene, describe their appearance and specify their location (on a recall grid). The remaining three recall scenes acted as distracters. Each recognition test was made up of 50 recognition targets and 50 recognition foils which were presented within a forced-choice recognition procedure. At test, participants were shown two scenes at a time and asked to judge which they had seen before, answering "A" or "B."

Each set of verbal tests comprised of three verbal stories devised by Isaac & Mayes (1999). Each story contained 20 units of information based around a different theme. At test, participants were required to recall as much about the story as possible. Recognition of each story was assessed using a series of twelve forced-choice questions each with four alternative answers (one correct, three similar foils) from which the participants had to pick the correct one. For copies of the stories refer to Appendix C.

Results

On the basis of piloting, the following amendments were made to the initial test materials and procedure.

Visual Tests

- Pilot 1 resulted in three recall scenes being removed from each set due to unacceptably poor recall and participants' comments that learning and distinguishing between 12 scenes was too difficult. To avoid ceiling effects found to be associated with the forced-choice recognition procedure, the format was changed to a 'yes-no' recognition procedure. A practise test was also

introduced to orientate participants to the requirements and acquaint them to naming things quickly.

- Pilot 2 revealed that recall of visual scenes was still unacceptably poor at the one-week delay. To ensure initial consolidation and avoid floor effects at the long-delay, this resulted in each recall scene being presented twice during the initial presentation. To increase the saliency of individual scenes, each was assigned a verbal label to be read aloud by participants. To increase the saliency of different elements within each scene, each scene was also spilt into quadrants. During presentation each section was outlined one at a time for one second during which time participants' were asked to name something within each section. The whole scene then remained on the screen for a further five seconds.

  Performance on the 'yes-no' recognition procedure was still close to ceiling at the short delays. To guard against this, the presentation time for each recognition target was reduced from 2 seconds to 1 second.

- The performance of the final two participants during Pilot 3 confirmed that the amendments successfully ensured initial consolidation and avoided ceiling effects at short delays and floor effects at the long delay.

Verbal Tests

Piloting confirmed that the stories were a sensitive test of forgetting over long delays with no evidence of floor or ceiling effects in the performance of pilot participants. The stories created by Issac & Mayes (1999) were therefore accepted with no amendments.

2. MATCHING SETS FOR DIFFICULTY

Participants

The 29 control participants (11 male, 18 female) from the main study took part in this phase of test development. Their demographic details can be viewed in Table 2 of the main report.

Method

To evaluate whether the final sets were matched for difficulty, all control participants were tested on both final sets using the procedure described in the main report. The presentation order was counterbalanced such that half received set A first, and half set B first. Test administration was spaced at least two months apart.

Results

Independent-samples t-tests using a Bonferroni adjusted alpha level confirmed that the final two sets were matched for difficulty. As can be seen in Table A overleaf, when the mean scores on each dependant variable was analysed separately at each delay there was no significant difference between sets ($p > 0.001$ in all cases). For completion, each variable was also collapsed across delay and the means were compared again. Again, using a Bonferroni adjusted alpha, there was no significant difference between groups ($p > 0.004$ in all cases). These results provided assurance that the tests will be suitable for future reassessment.

Table A. Set A vs. Set B: Mean performance of control participants compared

Experimental Test	Delay	Set A *Mean (SD)*	Set B *Mean (SD)*	T-test comparison *t*	*p-value*
Visual Tests					
Item Recall	Immediate	15.55 (2.13)	15.10 (2.48)	0.738	0.464
	30-minutes	14.24 (3.11)	13.72 (3.42)	0.602	0.549
	1-week	7.90 (3.85)	6.45 (3.46)	1.507	0.137
Spatial Recall	Immediate	6.79 (0.49)	6.61 (0.59)	1.285	0.204
	30-minutes	6.41 (0.88)	6.28 (0.98)	0.527	0.600
	1-week	4.53 (1.32)	3.73 (1.90)	1.872	0.066
Descriptive Recall	Immediate	81.23 (8.94)	77.08 (7.68)	1.899	0.063
	30-minutes	76.38 (10.66)	75.77 (16.65)	0.167	0.868
	1-week	67.51 (19.60)	58.10 (18.65)	1.873	0.066
Visual Scene Recognition (*d'*)	Immediate	3.61 (0.50)	3.88 (0.57)	-1.898	0.063
	30-minutes	3.18 (0.50)	3.60 (0.56)	-3.025	0.004
	1-week	1.92 (0.50)	1.82 (0.58)	0.702	0.405
Verbal Tests					
'Short-Delay Story' Recall	Immediate	13.03 (3.05)	12.28 (2.91)	0.968	0.337
	30-minutes	12.24 (3.40)	11.0 (2.78)	1.523	0.133
'Short-Delay Story' Recognition	Immediate	10.03 (1.86)	9.45 (1.78)	1.224	0.226
	30-minutes	9.93 (1.85)	9.07 (2.14)	1.642	0.106
'Long-Delay Story' Recall	Immediate	12.48 (3.76)	11.48 (2.95)	0.968	0.264
	1-week	7.86 (3.81)	7.28 (3.70)	0.667	0.501
'Long-Delay Story' Recognition	Immediate	10.21 (1.52)	9.52 (1.96)	1.498	0.140
	1-week	8.34 (2.27)	7.66 (2.09)	1.202	0.234

APPENDIX E

STATISTICAL FORMULAE

1. Modified t-test formula (Crawford & Howell,1998; Crawford & Garthwaite, 2002)

2. Corrected Measure of Spatial Discrimination

3. Corrected Measure of Descriptive Recall

4. Signal Detection Theory

1. Modified t-test formula

This formula (described by Crawford & Howell (1998) and Crawford & Garthwaite, (2002)) was deemed appropriate for comparing individual TLE participants with a control sample with a modest N. The approach treats the statistics of the control group sample as statistics rather than population parameters and uses the t-distribution (with N-1 degrees of freedom) rather than the normal distribution to test whether a patient's score is significantly lower than the scores of the control sample. The authors refer to the method as being a modified independent samples t-test in which the individual is treated as sample of N = 1, and therefore does not contribute to the estimate of within group variance. The formula is:

$$t = \frac{X_1 - \overline{X_2}}{S_2\sqrt{\frac{N_2+1}{N_2}}},$$

Where, X_1 = the individual's score, $\overline{X_2}$ = the mean of the normative sample, S_2 = the standard deviation of the normative sample, and N_2 = the sample size. The standard deviation refers to the estimated population standard deviation, that is, it should be calculated with *N*-1 in the denominator not *N*.

The computer program 'SINGLIMS' was downloaded from the first author's website at http://www.abdn.ac.uk/~psy086/dept/SingleCaseMethodsComputerPrograms.HTM to implement this procedure.

2. *Corrected Measure of Spatial Discrimination*

A corrected measure of spatial discrimination (see Hunkin et al., 1994) was required as recall of spatial information varied as a function of the number of items recalled. For example, if only one item was recalled but the participant remembered its spatial location, this would lead to a higher score (100%) than a participant who recalls six items but only recalls the correct spatial location for five of those items (80%).

Hunkin et al.'s discrimination score (*z*) is calculated as:

$$z = (r-x)/S.D.$$

where z = correct spatial responses; x = n.p.; n = number of items recalled; p = probability of recalling spatial information by chance; S.D.= square root of (n.p.q); and q = (1-p). In this case the probability of recalling spatial information by chance was computed as 0.25 as there were four potential locations on the grid.

3. Corrected Measure of Descriptive Recall

To account for the differences in the number of items recalled in the calculation of descriptive information, Muhlert (unpublished PhD thesis) devised a corrected measure of descriptive recall. This descriptive score *%d* was calculated as

$$\%d = ((d/2)/i)*100$$

where d = descriptive recall raw score (divided by 2 as it was scored up to two points for each item); i = item recall raw score. The score *%d* represents the percentage of descriptive information correctly recalled about the items remembered.

4. Signal Detection Theory

Visual scene recognition was scored using signal detection theory (see Macmillan & Creelman, 1991). The number of hits and false positives were taken into account by calculating an index of accuracy (d') and an index of bias (b).

Accuracy (d') was calculated using the formula:

$$d' = Z(\text{Yes/Signal}) - Z(\text{Yes/Non-signal})$$

where Z(Yes/Signal) is the standard normal deviate corresponding to the percentage of hits and Z (Yes/Non-signal) corresponds to the percentage of false positives. Higher accuracy is reflected by a higher value d'.

Bias (b) was calculated as follows:

$$b = (Z(\text{Yes/Signal}) + Z(\text{Yes/Non-signal})) / (-2)$$

A b value of zero indicates absence of bias, a positive b value indicates a bias towards responding "No" and negative b value this indicates a bias towards responding "Yes."

A standard correction was applied to deal with hit rates of 1 and false alarm rates of 0. Not counting zero, the smallest false alarm rate is 1/N as when you measure 0, the true false alarm rate falls between 0 and 1/N. Therefore, the standard method of correction is 1/(2N) instead of zero (this is the same as saying half a false alarm was observed).

In this study, N=50 (N refers to the maximum number of possible false alarms)

⟶ Standard method of correction = 1/(2N) = 1/100 = 0.01

Therefore the corrected false alarm rate = 0.01

The same reasoning was applied to a hit rate of 1.0 so that instead of using 1.0, the formula 1 – 1/(2N) was applied, where N is now the number of targets (50), the corrected hit rate therefore being 0.99.