Development of a New Test of Accelerated Long-Term Forgetting in Epilepsy

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Abstract

Accelerated long-term forgetting (ALF) is a novel form of memory impairment in which epilepsy patients demonstrate intact recall and recognition after standard delays, but they show an accelerated rate of forgetting in comparison to controls when the retention period is extended. ALF has been evidenced in children with idiopathic generalised epilepsy (IGE), who showed ALF for verbal material over a period of 1 week. Use of a minimum-learning criterion revealed that poorer initial learning was mediating the effect of ALF. The current study aimed to further investigate rates of forgetting in 5 children with IGE in comparison to 13 healthy controls, whilst developing a new spatial object-locations task to be used as a non-verbal measure of ALF. When tested immediately and at 30 minutes, memory for 2 stories was equivalent between groups but at 1 week there was a strong trend (approaching significance) for IGE participants to recall less verbal material than controls and there was a significant main effect of group and delay. IGE and control group participants did not differ in the number of trials required to reach criterion. Neither of the 2 measures of non-verbal, spatial memory revealed significant group differences, nor were there group differences in verbal or non-verbal recognition performance. The findings are interpreted in relation to previous research and theories of memory consolidation. Directions for future research and further development of the spatial object-locations task are considered.
1. Introduction

1.1 Epilepsy and Memory

Epilepsy is a neurological disorder encompassing a range of conditions that reflect underlying brain dysfunction. It is characterised by epileptic seizures during which the brain’s normal electrical activity is temporarily disrupted (Fisher et al., 2005). It is well-documented in the literature that epilepsy can have a detrimental impact upon cognitive functioning (Aldenkamp & Bodde, 2005; Fisher et al., 2000; McCagh, Fisk, & Baker, 2009). In particular, problems with memory are frequently reported by people with epilepsy (Corcoran & Thompson, 1992). Researchers have attempted to document the memory profile in epilepsy but efforts are complicated by several interrelated factors including age of onset, the brain pathology causing the seizures, the brain regions implicated by the epileptiform activity, lateralisation of seizure focus, interictal (time between seizures) epileptic discharges, severity and duration of the condition and the type and number of anti-epileptic drugs (AEDs) prescribed (Hendricks et al., 2004; Zeman, 2009). All of these factors may disrupt normal memory processes in some way, thus people with epilepsy can present with very specific deficits or more general memory impairment.

1.2 Childhood Epilepsies and Memory

Epilepsy is the most common neurological disorder to affect children and young people. It is well established that patients and their families complain of memory problems and a lack of progress in school, which often has a profound impact on social, cognitive and behavioural development and leads to educational underachievement (Aldenkamp, Weber, Overweg-Plandsoen, Reijs, & van Mil, 2005).

1.3 Memory Impairment in Epilepsy

Material-specific impairment in adults with lateralised epilepsy. Much of the data concerning memory in epilepsy has been obtained from samples of patients with focal epilepsy originating from the temporal lobes, in which structures such as the hippocampal system that are crucial for normal memory function are directly involved in seizure activity. In approximately half of temporal lobe epilepsy (TLE) cases, an overt lesion will be identified (Helmstaedter, 2008).
There is considerable evidence supporting the lateralisation of memory functions and the material-specificity of impairment as determined by hemispheric location of seizure focus (Golby et al., 2001; 2002; Pegna et al., 2002). In cases of dominant, left-sided TLE, verbal memory processes would be affected, whilst non-dominant right-sided TLE is associated with impaired memory for non-verbal (usually visuo-spatial) material. Giovagnoli and Avanzini (1999) investigated verbal and visual memory in patients with unilateral lesional or cryptogenic (epilepsy of unknown cause but where a physical explanation, such as a lesion, is suspected) TLE and healthy controls. Memory for verbal material was consistently poorer in patients with left-sided TLE than controls. Amongst epilepsy patients, those with left cryptogenic TLE were impaired relative to all right-sided patients on immediate word-list recall. Delayed recall performance of the left lesional group was worse than all right TLE patients on the word-list measure and poorer than the right lesional patients for the story. Visual memory measures did not show such compelling results, nevertheless memory for 10 abstract designs was significantly worse in the lesional right TLE patients than controls and all right TLE and left lesional TLE epilepsy groups were impaired relative to controls in their the ability to reproduce a complex meaningless picture after a 1 hour delay. These findings suggest that the integrity of verbal memory processes are diminished in left TLE and that non-verbal memory is also vulnerable in epilepsy, perhaps more so in right TLE.

Abrahams, Pickering, Polkey, and Morris (1997) conducted a study which independently investigated object and spatial memory in patients with intractable TLE and patients who had undergone unilateral temporal resection. Their task encouraged participants to remember the locations of objects hidden in containers on a board in relation to cues in the environment rather than in relation to their personal perspective, because they were asked to move to different positions around the board prior to recall. Performance did not differ between TLE and resection patients, but all those with right temporal lobe damage were selectively and markedly impaired on the spatial memory components of the task. Left-sided TLE and resection patients were as capable as controls at recalling spatial information. Patients’ non-spatial working memory was comparable to controls, although they were poorer at remembering the 2 objects that were repeatedly hidden across trials. Findings were replicated in a larger sample of TLE patients (Abrahams et al., 1999), moreover the degree of spatial memory impairment correlated with patients’ hippocampal and parahippocampal
gyrus volumes. Collectively, these studies support the lateralisation of spatial memory processing within the right hemisphere.

There is growing evidence that questions the strict verbal versus non-verbal hemisphere distinction (Kennepohl, Sziklas, Garver, Wagner, & Jones-Gotman, 2007; Saling, 2009). It has been proposed that the lateral and mesial portions of the temporal lobes perform different functions for learning, memory and recognition. Helmstaedter, Grunwald, Lehnertz, Gleissner and Elger (1997) revealed that temperolateral structures were material-specific and associated with processing information in working memory, with the left lateral temporal lobe preferentially involved in learning verbal material. However, epilepsy originating in the mesial temporal lobes, in which the hippocampi reside, was associated with an impaired ability to consolidate, retain and retrieve material from long-term memory, independent of the material type. These findings suggest that memory impairment in epilepsy should not be limited to a verbal or non-verbal definition, since there are cortical regions involved in memory processes that are material non-specific. It might also offer some explanation for the less uniform results on the non-verbal memory measures in Giovagnoli and Avanzini’s (1999) investigation.

**Material-specific impairment in children with lateralised epilepsy.** Despite limited studies comparing children with right- and left-lateralised seizure focus, the evidence for material-specific impairment is weak (for a review see MacAllister & Schaffer, 2007). Gonzalez, Anderson, Wood, Mitchell, and Harvey (2007) investigated the localisation and lateralisation of memory deficits in children with TLE using a comprehensive range of verbal and non-verbal tasks. Memory for semantically related and unrelated verbal material was assessed whilst non-verbal measures to tap spatial memory, face recognition and picture recognition were administered. A further non-verbal task called the Rey-Osterrieth Complex Figure Test (ROCFT), in which patients must copy and reproduce an abstract drawing from memory, was also used. None of these revealed a tendency for left-sided TLE patients to be poorer in the verbal domain relative to right-sided TLE. Right-sided patients did not show more severe non-verbal memory deficits, apart from performing worse on delayed facial recognition. Interestingly, Engle and Smith (2010) proposed that in children, attentional ability may mask material-specific deficits. They observed correlations between attention and delayed verbal memory but not visual memory in those with seizure focus in the right hemisphere, whereas in left-sided patients,
attention correlated with delayed visual memory only. Perhaps in paediatric populations, aetiological factors do impair memory for specific types of material but significant attention difficulties cause more diffuse memory dysfunction.

**Verbal and non-verbal impairment in adults.** Verbal-oriented memory problems are widely accepted as a likely outcome of left-sided focal epilepsy (Aikia, Salmenpera, Partanen, & Kalviainen, 2001; Hendricks et al., 2004) but they also arise in the non-focal epilepsy syndromes in which seizure activity involves both hemispheres of the brain. Taylor et al. (2010) investigated memory in patients with focal, generalised and unclassified epilepsy and compared to controls, all groups were equally less able to recognise abstract visual stimuli, they recalled fewer words from a verbal learning task under immediate and delayed conditions, and their delayed story recall was significantly worse. A 5-year follow-up of the same cohort (Taylor & Baker, 2010) indicated that this pattern of impairment persisted. Scores on the verbal learning task actually declined which is corroborated by other longitudinal studies reporting progressive decline of verbal memory in epilepsy (for a review see Seidenberg, Pulsipher & Hermann, 2007).

However, greater prevalence of visually-based memory problems has been demonstrated in non-focal epilepsy (Helmstaedter, 2008; Hommet, Sauerwein, De Toffol, & Lassonde, 2006). Dickson, Wilkinson, Howell, Griffiths, and Grunewald’s (2006) participants were people diagnosed with idiopathic generalised epilepsy (IGE), which encompasses a range of syndromes thought to have a genetic basis with generalised seizures occurring in the absence of organic brain damage. They demonstrated memory impairment in both the recall and recognition components of several non-verbal tasks. Using the Doors and People test of long-term memory, their visual recognition memory of photographs of doors and delayed recall memory for visual patterns was impaired relative to healthy controls. Immediate recall of a complex figure and face recognition ability was also significantly worse in the epilepsy group. Signs of verbal memory impairment were only revealed during delayed recall on 1 measure. Interestingly, if verbal memory impairment is present, delayed recall seems to be most affected (Aikia, Kalviainen, & Riekkinen, 1995).

**Verbal and non-verbal impairment in children.** Typically, children with focal TLE exhibit the most significant, widespread difficulties. Those with generalised seizure activity may only differ from healthy children on 1 or 2 measures, commonly those that assess memory for visually-based material (Nolan et al., 2004).
Bailet and Turk (2000) found that children with idiopathic epilepsy were impaired during immediate recall of both verbal and visual material compared to their siblings who served as controls and children with migraine. They also made significantly more errors during complex figure recall than controls. Analysis did not reveal any differences between patients with complex partial (focal seizure with partial loss of consciousness) or generalised seizures.

In a group of patients diagnosed with absence seizures or generalised tonic-clonic seizures (GTCS) (both IGE syndromes), Henkin et al. (2005) observed only verbal memory impairments. Those with absence seizures performed significantly worse than healthy controls on all but 2 subscales of the California Verbal Learning Test (CVLT) which involves learning and recalling a list of words across 5 trials, learning a distracter list of words followed by delayed recall, cued recall and recognition of the original word-list. Children with GTCS were impaired on 2 subscales only. The authors also calculated the number of words participants had to actively search for in memory during the recognition component of the CVLT. Patients with absence seizures were shown to have difficulties retrieving verbal material from memory. The number of words retained between immediate and delayed recall did not differ between groups, suggesting that inefficient learning may also have contributed to poorer recall. Using the ROCFT to investigate non-verbal memory, no group differences were observed.

Selective deficits in non-verbal memory have been evidenced in children with IGE. Jambaque, Dellatolas, Dulac, Ponsot, and Signoret (1993) found that relative to controls, the epilepsy group were impaired on every measure of visual memory which included immediate and delayed geometric figure recall, immediate and delayed design list recall, figure recognition and figure associated pairs. During this task, pairs of figures are memorised and for recall, 1 figure is presented and the associated figure must be selected. Nolan et al. (2004) compared memory functioning in children with childhood absence epilepsy (CAE), TLE and frontal lobe epilepsy (FLE). Although CAE patients were least impaired overall, when compared to standardised norms they were significantly poorer on a non-verbal memory task requiring working memory and sustained visual attention and on a measure of visuo-spatial memory. Again, verbal memory was within the range expected of a healthy population. More recently, Volkl-Kernstock, Willinger, and Feucht (2006) conducted a study focusing on spatial functions in patients with benign childhood epilepsy with centro-temporal spikes.
(BCECTS). Patients demonstrated short- and long-term spatial memory impairments in their ability to recall a visuo-spatial array and rebuild figures constructed from building blocks over multiple trials and following delays. In BCECTS, formerly known as rolandic epilepsy, the epileptic focus in the parieto-temporo-occipital regions. Volkl-Kernstock et al. (2006) identified no differences in the degree of spatial memory impairment between children with focus in the left or right hemisphere. This finding may be due bilateral epileptiform activity which occurs in BCECTS, but this also assumes that both hemispheres are involved in processing spatial information.

There are various factors potentially impacting upon memory performance. Other than the relatively consistent findings from focal studies concerning material-specificity of the right and left hemispheres, much variability remains concerning the presence or absence of memory deficits, the type of material affected and the memory processes responsible for producing impairment.

1.4 Executive Functioning in Epilepsy

Executive functioning in adults with epilepsy. There is general consensus that executive functions (EFs) are compromised in FLE (for a review see Patrikelis, Angelakis, & Gatzonis, 2009). Patients with FLE have been found to perform poorly on tasks requiring response selection, behavioural initiation and maintenance, attention, cognitive flexibility, sequencing and response inhibition (Farrant et al., 2005; Helmstaedter, Kemper, & Elgar, 1996; McDonald et al., 2005; Upton & Thompson, 1996). An inability to divert attention away from interfering stimuli and suppress automatic, habitual responses appear to be most characteristic of FLE cognitive impairment, since this can differentiate between FLE and TLE patients (Helmstaedter, 2001a).

Others argue that TLE patients are equally vulnerable to executive dysfunction (Exner et al., 2002). Hermann, Seindenberg, Lee, Chan, and Rutecki (2007) identified 3 distinct cognitive profiles in their TLE sample, 2 of which included impaired performance on measures of EFs. Patients classed as ‘minimally impaired with normal IQ’ performed poorly on task involving problem-solving, response inhibition, visual attention and task switching. In the ‘moderately to severely impaired’ group,
executive functioning as well as psychomotor speed and memory were significantly below their mean IQ.

**Executive functioning in children with epilepsy.** Patients with idiopathic generalised and idiopathic partial epilepsy syndromes might also present with executive deficits (Hommet et al., 2006). Devinsky et al. (1997) found that around 50% of participants with juvenile myclonic epilepsy (JME) were mildly impaired compared to a matched group with TLE on measures of planning, cognitive flexibility and abstract reasoning. The remaining 50% were more severely impaired on these tasks. More recently, Piazzini, Turner, Vignoli, Canger, and Canevini (2008) administered a word fluency task and the Wisconsin Card Sorting Test (WCST) as a measure of cognitive flexibility to patients with JME, FLE, TLE and controls. Those with JME performed similarly to the frontal group and they were both significantly worse than TLE patients and controls on all measures. TLE patients were no different to controls in terms of the number of card categories they sorted or word fluency performance.

A considerable number of people with epilepsy may be at risk of executive dysfunction, but the degree of impairment is most acute in FLE. Significant impairment has also been documented in non-focal epilepsies, with lesser deficits apparent in TLE.

**1.5 Accelerated Long-Term Forgetting**

In clinical practice, epilepsy patients who report experiencing memory problems will undergo a thorough neuropsychological assessment with the aim of quantifying their subjective complaints. Despite mounting evidence of memory impairment in epilepsy, there is some indication that their performance on standardised memory tests is disproportionate to those reports and at times within the range expected by a normal population (Corcoron & Thompson, 1992; Hemlstaedter, 2001b; Piazzini, Canevini, Maggiori, & Canger, 2001). This discrepancy has been investigated further by using more experimental methods that measure memory retention beyond the scope of time-constrained conventional tests. Consequently, a novel form of memory impairment has been observed in some patients with epilepsy. Patients show apparently normal learning and intact recall and recognition of material after standard delays of around 30 minutes, but they show an abnormally accelerated
rate of forgetting in comparison to healthy participants when the retention period is extended (for reviews see Bell & Giovagnoli, 2007; Butler & Zeman, 2008).

Traditional models of memory have encouraged the assumption that information stored for longer than a few minutes has reached long-term memory and is no longer being processed in working memory. Questions about the nature of the processes operating between the time of initial learning and retrieval of information have been relatively neglected. As Squire and Alvarez (1995) speculated on cases of temporally graded retrograde amnesia, if it is possible for memories acquired much further into the past to be more preserved than those recently formed, then the consolidation of memory must extend beyond a brief period and could continue gradually, for weeks, months or even years after learning. Accelerated long-term forgetting (ALF) is likely to be a disorder of memory consolidation. Those who demonstrate this pattern of forgetting achieve normal memory performance after delays of around 30 minutes which suggests that they are capable of acquiring information effectively. The discovery of ALF offers new insight into the processes underlying long-term memory consolidation. It provides evidence for an extended period of vulnerability, during which memories gradually become more resistant to decay and disruption as they undergo a dynamic multiple-staged consolidation process before reaching permanent storage. Research that has identified ALF in epilepsy will be discussed here.

**Single-case studies.** A selection of individual case studies of non-surgical patients with TLE provide informative accounts of the ALF phenomenon (Kapur et al., 1997; Mayes et al., 2003; O’Connor, Sieggreen, Ahern, Schomer, & Mesulam, 1997).

O’Connor et al. (1997) described J.T whose performance in non-memory domains was at best, in the superior range and at worst, in the low average range when seizure frequency was high. Verbal and non-verbal memory abilities were intact, though when performance was poorer than expected it was attributed to an increased number of seizures. Verbal memory tests were adapted in order for long-term forgetting to be monitored over 2 hours, 24 hours and 1 week. His immediate recall of a list of words was perfect and recall at 2 hours was identical to that of his brother who served as a control comparison. When tested the following day, J.T’s memory for the word list had suffered a dramatic reduction and after a further 2 hours
he was performing at floor. After 1 week, he could not remember any words, whereas his brother retained 80% of the list.

Patient P.A., who was also diagnosed with TLE, demonstrated ALF over the course of 6 weeks (Kapur et al., 1997). Her general cognitive ability consistently ranked within the range expected of a normal population, yet very long-term memory was markedly impaired. In comparison to matched, healthy participants, immediate and 30 minute story recall was equivalent. Non-verbal memory was assessed using a visual design task in which a set of abstract drawings were to be reproduced at the specified intervals. With this material, her memory was also the same as controls when tested up to 30 minutes. After 6 weeks however, she had retained none of the story or any of the designs. Interestingly, her verbal recognition memory was poor yet she performed as well as controls during the recognition component of the visual task.

The single-case literature offers detailed portrayals of the key features of ALF but their finding are not easily generalisable. Epilepsy was not the only possible explanation for the observed memory impairment; traumatic head injury had pre-dated seizure onset (Mayes et al., 2003), epilepsy occurred in conjunction with a rare form of encephalitis (O’Conner et al., 1997) and where there was no identifiable cause, the TLE diagnosis was made very late in the patient’s life (Kapur et al., 1997). This limits the certainty with which we attribute ALF to epileptiform activity. The mixed structural pathology of the cases, which included the presence (Kapur et al., 1997) and absence (Mayes et al., 2003) of hippocampal damage, also prevents speculation as to which regions produce the impairment.

**Group studies.** Investigations benefiting from larger samples of epilepsy patients and matched healthy controls have revealed mixed findings; the occurrence of ALF has been both confirmed (Blake, Wroe, Breen, & McCarthy, 2000; Davidson, Dorris, O’Regan, & Zuberi, 2007; Helmstaedter, Hauff, & Elgar, 1998; Mameniskiene, Jatuzis, Kaubrys, & Budrys, 2006) and contradicted (Bell, Fine, Dow, Seidenberg, & Hermann, 2005; Giovagnoli, Casazza, & Avanzini, 1995).

TLE patients studied by Mameniskiene et al. (2006) performed immediate and delayed recall of a word list and a story and non-verbal memory was assessed using the ROCFT. Even during immediate recall and at standard delays of 30 minutes, patients showed impaired memory performance compared to controls. Long-term memory was tested after 4 weeks had passed and again, the TLE group were significantly poorer on all measures. Although ALF is best illustrated when memory
is intact at standard delays, which was not the case here, patients forgot much more material between the shorter and longer intervals than controls. The authors calculated how much of the information recalled at 30 minutes had been retained by each group over the 4 weeks and TLE patients remembered between 20-30% less than controls. For example, patients recalled approximately 25% of what they had remembered of the word list when tested at 30 minutes, whereas healthy participants typically recalled almost 60%. Despite evidencing memory impairment under all conditions, the TLE group seemed to show rapid forgetting of what they were able to recall at standard delays.

More convincing results were reported by Blake et al. (2000) in a group of focal epilepsy patients who showed ALF of verbal material following an 8 week delay. All participants showed a normal capacity to remember a short story when recall was examined at 30 minutes and the very long delay caused both groups to remember significantly less. However, after 8 weeks, the epilepsy patients’ recall and recognition was much worse than controls and the amount they had forgotten over the extended delay was differentially poorer than the control group. A crucial factor that Blake et al. (2000) considered in their experimental procedure was the role of initial learning and the effect it may have on subsequent recall performance. To ensure that everyone learned the material to an equivalent level, stories were repeatedly presented until participants obtained a recall accuracy of 90-100%. They were permitted a minimum of 2 and a maximum of 10 trails to reach this learning criterion. This method allows you to draw more meaningful conclusions from participants’ pattern of forgetting, since all participants have the same amount of information to consolidate over the extended delay period. Setting a learning criterion is also a means of investigating long-term forgetting in those who are short-term memory impaired. When recall is already impaired at standard delays (Bell et al., 2005; Helmstaedter et al., 1998; Mameniskiene et al., 2006), it is difficult to reject the possibility that ALF is attributable to poorer initial acquisition which leaves a reduced amount of information to be retrieved during later recall. Nonetheless, selecting the appropriate method by which to equate learning is important because repeated exposure to material may also cause over-learning (Butler & Zeman, 2008).

Thus far, there is a strong indication that ALF is most typically observed in people with epilepsy. There is less agreement as to where in the sequence of memory processes the deficit arises i.e. during encoding, consolidation or retrieval. Patients
and controls in Blake et al.’s (2000) study did not differ in the number of trials needed to reach the learning criterion, however the inefficient encoding ability of a group of children with IGE seemed to be producing their ALF at long-term recall (Davidson et al., 2007). On the whole, rapid forgetting is evident during both recall and recognition components of memory tasks, suggesting that memories are lost during the extended delay (Butler, Muhlert, & Zeman, 2010). Conversely, Davidson et al.’s (2007) IGE sample performed recognition as well as healthy controls, but a selective difficulty retrieving information from memory is unlikely because their ALF was attributed to poor learning. It also remains to be clarified which types of material are affected.

Mameniskiene et al.’s (2006) patients were memory-impaired for both verbal and visual material, whereas Blake et al. (2000) found evidence for material-specificity. They conducted a comparison between patients with left- versus right-sided seizure focus. Left hemisphere patients were significantly poorer at story recall following the 8-week delay only and there was no difference between right-hemisphere patients and the control group.

**Transient epileptic amnesia.** A newly recognised form of TLE affecting middle-aged to elderly people is transient epileptic amnesia (TEA), in which seizures are visible as brief but frequent episodes of amnesia. There will often be other evidence to support a diagnosis of epilepsy such as abnormal epileptiform activity on wake or sleep electroencephalography (EEG) recording and the majority of those diagnosed will respond to AED treatment (Butler et al., 2007; Zeman, Boniface, & Hodges, 1998).

In all cases of TEA, patients describe persistent memory problems that affect their everyday lives which are supplementary to the transient amnesic attacks. Manes, Graham, Zeman, de Luja´n Calcagno, and Hodges (2005) investigated whether the ALF phenomenon that had been observed predominantly in cohorts of TLE patients, might also affect those with TEA. They used story recall and recognition to probe verbal memory and to test non-verbal memory, participants were required to reproduce and recognise a set of line drawings. Memory was assessed at standard delays and again after a long-term interval of 6 weeks. There were no differences in patients and controls’ immediate or 30 minute verbal recall and both groups forgot a significant amount of the story over 6 weeks, yet there were marked group differences at the extended delay. The TEA group remembered significantly less than healthy
controls at 6 weeks and the pattern of performance during recognition was similar. The authors found no evidence for ALF of visual material.

A thorough analysis of ALF in TEA was conducted by Butler et al. (2007). Of 50 patients, they selected those who had performed within the normal range on standard memory assessments and administered a word-list learning task and a non-verbal design-learning task with recall and recognition tested at 30 minutes, 1 week and 3 weeks. They also incorporated a learning criterion which required participants to reach 90% accuracy within 15 trials and at least 5 trials were given initially; there were no group differences with regard to learning efficiency. Patients remembered less than controls during word-list recall at 30 minutes but they forgot a considerable amount of material over the following week, which the healthy group did not. Recall at 3 weeks did not show much of a change from performance at 1 week. Memory for visually presented designs was comparable amongst all participants 30 minutes after the last learning trial, but a group difference emerged between the 1st and 3rd week. Butler et al. (2007) identified that TEA patients’ forgetting rate was different to that of controls and their verbal and non-verbal recall memory was significantly poorer over the 3 week delay. Interestingly, when they conducted separate comparisons between controls and patients who had and had not complained of experiencing accelerated forgetting, the previously observed interactions were only evident between patients with subjective memory complaints and controls. This suggests that a sub-group of TEA may be particularly vulnerable to AFL.

Memory functioning is predominantly explored using standardised measures that investigate memory for verbally-based material using word-lists and stories and non-verbal memory using visual abstract designs, line drawings and complex figures for example. Muhlert, Milton, Butler, Kapur, and Zeman (2010) attempted to find out whether memories for real-life events would be subject to ALF in patients with TEA, in whom reports of everyday memory difficulties are common. Participants wore a camera to capture their day-to-day activities, which was used to create more ecologically valid stimuli for memory testing. Patients and controls did not differ in their same-day recall of events but the TEA group forgot more rapidly over 3 weeks as revealed by their next-day, 1 week and 3 week recall. Patient’s recall for other contextual details about the event, such as the temporal context and associated thoughts, deteriorated in a similar fashion following normal memory performance at same-day recall. Forgetting in patients was significantly greater between the same-day
and 1 day delay, suggesting that in this sample, ALF of memories for real-life events was most prominent over the first 24-hour period following encoding.

**Causes.** Collectively or alone, a number of epilepsy-related factors might produce ALF, but the extent to which they contribute has not been determined. Epileptiform activity could disturb memory processes, the pathology causing the seizures may independently result in memory problems, or ALF may be an adverse side-effect of AEDs.

Patient J.T (O’Connor et al., 1997) endured exceptionally frequent seizures and variability in his memory performance appeared to correlate with the number of seizures observed prior to testing. Of Mameniskiene et al.’s (2006) TLE patients, those who had a seizure between the 1st and 2nd testing session were poorer at long-term recall and showed ALF of verbal material compared to those who did not. Performance also differed depending on seizure severity; patients with seizures causing partial loss of consciousness were worse at long-term recall than patients who remained fully conscious. Furthermore, higher seizure frequency correlated with poorer recall memory and ALF of verbal material at 4 weeks. Specifically examining the effects of seizures on rate of forgetting, Jokeit, Daamen, Zang, Janszky, and Ebner (2001) observed that left TLE patients showed ALF for word positions if they experienced a seizure during a 24-hour interval. Of those who were seizure-free, less than half showed impaired memory. However in TEA patients, whose AED treatment often eliminates seizures, ictal activity is unlikely to cause ALF (Manes et al., 2005). An area of some contention concerns the role of subclinical seizure-like activity that is visible on interictal EEG recording. Butler et al. (2009) found no relationships between seizure variables and ALF, but noted that amnesic attacks associated with TEA often occur on waking and suggested that subclinical epileptic discharges active during sleep may disrupt memory consolidation.

It is quite possible that overt lesions within the temporal lobes contribute to memory impairment, but it difficult to ascertain how they might independently produce such a specific deficit as ALF. In many studies, hippocampal sclerosis was not widespread (Blake et al., 2000; Butler et al., 2007) and the presence of temporal lobe lesions did not influence recall memory when assessed after an extended delay (Mameniskiene et al., 2006). Manes et al. (2005) considered that the prevalence of vascular changes on their TEA patients’ magnetic resonance imaging (MRI) to be a possible cause of ALF. They also suggested that the episodes of amnesia themselves
might induce dysfunction of the temporal lobes. Using manual and automated volumetric MRI, 1 study to directly explore brain atrophy as a cause of ALF did not determine that any clear relationships existed (Butler et al., 2009). Neither did the TEA patients’ hippocampal volumes, which showed subtle atrophy compared to controls, nor their medial temporal lobe volumes correlate with rates of forgetting over a 3-week period.

AEDs control the incidence of seizures but the drugs themselves might exacerbate memory problems (for a review see Motamedi & Meador, 2004). Jokeit, Kramer, and Ebner (2005) looked at the independent effects of AEDs on forgetting, although not at very long-term delays. Patients with TLE receiving monotherapy and were grouped according to their AED serum levels. Immediate recall of 2 stories and geometric figures was not related to the type of AED nor participants’ high or low serum levels. However, the amount of material they retained until memory testing at 30 minutes (verbal) and 60 minutes (non-verbal) bore no relation to laterality of seizure focus, gender, age, IQ, duration of epilepsy or seizure frequency; high and low AED serum levels were the sole determinant of superior and poorer recall performance, respectively. Conversely, when considering the literature reviewed above, ALF is often a presenting symptom in cases where AED treatment has not yet been initiated (Butler et al., 2007) and ALF persists even in less medicated populations (Davidson et al., 2007).

1.6 Accelerated Long-Term Forgetting in Children with Idiopathic Generalised Epilepsy

Onset of IGE is commonly in childhood and adolescence. Briefly introduced above, it encompasses a range of common syndromes thought to have a genetic basis with bilateral seizure activity occurring in the absence of structural lesions. They are usually responsive to AEDs. In comparison to other epilepsies, IGE has been associated with milder cognitive impairment and normal IQ (Beghi, Beghi, Cornaggia, & Gobbi, 2006). Children with IGE provide an opportunity to study the effects of epileptic activity on memory in a less medicated and perhaps less severely impaired population, and importantly, in isolation from the effects of organic brain damage.

The lack of consensus regarding memory impairment in IGE and the emergence of ALF in some adults with epilepsy prompted Davidson et al. (2007) to
study very long-term memory in a paediatric epilepsy sample. Participants included 21 children aged 8-16 years and controls matched for age and IQ. Verbal and non-verbal subtests taken from the Children’s Memory Scale (CMS) were administered according to standardised procedure. To investigate rates of forgetting over an extended interval, participants’ recall and recognition memory were re-assessed after 1 week. The authors found that children with IGE performed recall as well as controls following a standard 30 minute delay, but they demonstrated ALF for verbal material over the subsequent week. Recognition memory was comparable between patients and controls at standard and extended delays, which might have suggested that the IGE patients experienced difficulties retrieving successfully stored material from memory. Further analysis however, revealed that that poorer initial learning caused the accelerated forgetting of verbal material at 1 week. No differences were found in participants’ ability to learn and recall visuo-spatial information, in other words rates of forgetting for non-verbal material were comparable between children with IGE and controls.

Davidson et al.’s (2007) exploratory study produced some interesting findings. In contrast to other research which proposes that ALF it is most likely a disorder of memory consolidation, here, participants were unable to acquire the verbal material effectively. Larger samples of children with IGE are needed to corroborate the presence of ALF in childhood epilepsy and identify its causes. The lack of group differences in memory for non-verbal material might be reviewed since their only measure of visual memory used a simple grid system in which participants are required to learn the positions of counters. During recall, participants were instructed to guess if uncertain about a placement, but it was always likely that some would make a correct placement by chance because the number of counters was equal to half the available squares in the grid. An alternative non-verbal memory measure is needed to clarify whether children with IGE do not have a visual memory impairment, or whether the over-simplistic task masked a deficit.

1.7 The Current Study

The current study will replicate Davidson et al.’s (2007) procedure and build upon the methodology by incorporating a new non-verbal measure of ALF. 

**Introduction of a new spatial object-locations task.** The spatial object-locations test is a typical non-verbal memory measure, involving the encoding and
retrieval of spatial representations. It was adapted by Smith and Milner (1981; 1989) from Mandler, Seegmuller and Day (1977) (as cited in Smith & Milner, 1981; 1989) to explore the role of the right hippocampal region during learning and recall of the locations of 16 toys objects. Smith and Milner (1981) demonstrated that patients who had undergone right temporal resection were impaired relative to patients with left temporal resection and healthy controls, in their attempts to recall objects’ spatial locations. Their impairment was evident at recall and persisted, but did not deteriorate, when recall was performed again 24-hours later, strengthening the premise that these patients were unable to encode the object-locations effectively. The fact the left temporal lobe patients were able to perform recall as well as controls and right-sided patients were unable to verbalise the task suggests that it isolates non-verbal memory processes. In this study, participants performed a separate task prior to recall of the object-locations, and so in a subsequent study, Smith and Milner (1989) assessed recall immediately following exposure to the array of objects. On this occasion, right temporal resection patients were not impaired in their ability to recall object-locations, indicating that initially, they are able to encode the spatial information but it is not retained over time because performance was impaired at 30 minute recall.

This task recently underwent further modification and was piloted with a healthy adult cohort in which 10 toy objects were presented in a spatial array after which recall was tested. As Pentland, Anderson, Dye, and Wood (2003) noted when examining their adaptation of a spatial memory task for use with children, children’s ability to associate object and location develops slower than their capacity to remember object and location separately. Therefore, it is important to consider how they may represent spatial information in memory and how learning of the object-locations might be encouraged to enable them to perform recall after standard and very long-term delays. All participants view the array of objects from 1 position and are likely to encode the object-locations in relation to their personal perspective (Jagaroo, 1999). However it is also likely that they will represent the locations of objects in relation to neighbouring objects within the array, thus each object-location serves as a coordinate reference to others (Jagaroo, 1999; Pentland et al., 2003). Burgess, Maguire, and O’Keefe (2002) stated that egocentric and allocentric processing of spatial locations may be utilised in parallel, in order for information to be sufficiently remembered for subsequent recall. To investigate rates of forgetting of
non-verbal information across an extended delay, ensuring that learning of the object-locations takes place is important. On the other hand, Smith and Milner (1989) found that recall performance was not differentially affected by effortful as opposed to incidental encoding of object-locations. Nevertheless in their child sample, Pentland et al. (2003) instructed participants to familiarise themselves with the stimuli to control for attentional factors. To investigate children’s forgetting rates of non-verbal information across an extended delay, encouraging learning of the object-locations might reduce the possibility of participants performing at floor level.

1.8 Aims and Hypotheses of the Current Study

The ALF research is relatively recent and only 1 paper exists investigating ALF in children with IGE, therefore the current study is exploratory in nature and seeks to further investigate rates of forgetting in children with IGE and healthy controls. The spatial object-locations task will be developed in a series of pilot studies and its efficacy will be evaluated in comparison to an established, standardised non-verbal memory measure. The study will investigate whether administering a new spatial object-locations task will reveal a difference in the way children with IGE and healthy children remember non-verbal material.

The first hypotheses are derived from Davidson et al.’s (2007) findings:

- Children with IGE will require significantly more learning trials to reach criterion than controls.
- Immediate recall and recall at 30 minutes will be comparable between groups, but children with IGE will exhibit accelerated rates of forgetting and recall significantly less material at 1 week.
- ALF will be mediated by the number of learning trials, and thus due to inefficient encoding.

However, if children with IGE do not require significantly more learning trials than controls, there must be an alternative explanation for the occurrence of ALF:
• If learning is comparable between IGE patients and controls and recognition is intact, ALF is due to retrieval difficulties.

• If learning is comparable between IGE patients and controls and recognition is impaired, ALF is due to failed consolidation.
2. Method

2.1 Ethics

The study was approved by the West of Scotland Research Ethics Service at the Western Infirmary, Glasgow and permission to conduct research at the Royal Hospital for Sick Children, Edinburgh was obtained from the Research and Development Department at the Royal Infirmary of Edinburgh. Permission to recruit via local schools was granted by the Schools & Community Services section of Edinburgh City Council’s Children & Families Department (see relevant documents in Appendix A).

2.2 Pilot 1

Aims. The first pilot was conducted to assess the suitability of the spatial object-locations task for use with children and to ascertain an appropriate learning criterion. In the main study, memory for object-locations would be tested at extended delays and rates of forgetting compared, thus setting a learning criterion ensures that all participants retain equivalent amounts of information following initial exposure to the array. The aim of this pilot was to measure how accurately participants placed objects during recall and how many times they needed to view the array in order to make their most accurate placements. For the learning criterion, it was then possible to estimate how well children might be expected to perform recall of the object-locations and the number of trials they would be permitted to achieve that level of performance.

Method.

Materials. The spatial object-locations task required participants to learn the positions of 10 small toy objects (see Appendix B for list of toy objects) presented in a spatial arrangement on a white 60x60cm board. The array was depicted by 10 small green dots on which the centre of each object, also marked by a green dot, was placed (array shown in Figure 1). The toys are positioned in such a way so that their placement appears random and no obvious pattern can be detected. In a previous pilot using this task, objects were presented in 5 different spatial arrangements. The 2 arrays which adult participants found easiest to remember were used in the current pilot. Participants performed recall of the object-locations onto white sheets of paper of the same dimensions as the original board, using an identical set of toy objects.
Participants. Six children (2 male, 4 female) with a mean age of 8.75 years (S.D. = 1.05; range 7.5–10).

Procedure. Participants were instructed to memorise where the toy objects was placed on the board and informed that they would be asked to perform recall of the object-locations (see Appendix C for instructions). To encourage learning, participants were asked to name each of the objects. After 1 minute, the board was removed from view and a blank sheet of paper and an identical set of toy objects were placed in front of participants for them to perform recall of the object-locations. The 1 minute viewing duration was determined by the procedure in a previous pilot in which participants were asked to estimate the price of each object, which is likely to have taken participants around 1 minute. The pace was also kept fast enough to reduce the time participants had to think over-elaborately about the objects. Following recall, the original board, complete with toys in their assigned locations, was placed in front of them. On all subsequent trials, participants were given 30 seconds to view the board. Meanwhile, the experimenter used a pencil to mark where participants placed the objects during recall. Participants viewed the array of toy objects and performed recall of the object-locations 10 times.
Results. Object displacement scores were calculated by measuring the distance in millimetres between the centre of each object as recalled by the participant and the objects’ original position in the array. A mean displacement score was derived for each toy object across the 10 trials, as was an overall mean displacement score for each array. Data is presented in Table 1. The array with the lowest mean, which participants remembered most accurately, was used in the subsequent studies. The mean displacement measurement of this array was 34mm, in other words, participants placed each toy object at an average distance of 34mm from its fixed position in the original array. To ascertain a learning criterion, it was necessary to identify object displacements across trials as correct or incorrect until adequate learning had been achieved. The mean displacement of 34mm was chosen as the maximum radius measure within which participants would be required to place the 10 toy objects during recall. A stencil was produced which could be used to determine whether participants’ placements were within this radius (see Figure 2 and Appendix D for images of stencil). Placements beyond it would be scored as incorrect.

Using this new criteria, a second pilot was conducted to assess participants’ memory for the object-locations at delays of 30 minutes and after an extended delay of 1 week.

Table 1.
<table>
<thead>
<tr>
<th></th>
<th>Array 1</th>
<th>Array 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panda</td>
<td>37.4*</td>
<td>36.4</td>
</tr>
<tr>
<td>Yellow man</td>
<td>38.5</td>
<td>47.8</td>
</tr>
<tr>
<td>Dice</td>
<td>32.3</td>
<td>51</td>
</tr>
<tr>
<td>Car</td>
<td>32.3</td>
<td>22.9</td>
</tr>
<tr>
<td>Watch</td>
<td>34.8</td>
<td>31.6</td>
</tr>
<tr>
<td>Duck</td>
<td>18.9</td>
<td>38.9</td>
</tr>
<tr>
<td>Strawberry</td>
<td>37.7</td>
<td>57.3</td>
</tr>
<tr>
<td>Banana</td>
<td>29.3</td>
<td>50.4</td>
</tr>
<tr>
<td>Key</td>
<td>42.3</td>
<td>57.3</td>
</tr>
<tr>
<td>Frog</td>
<td>37.7</td>
<td>48</td>
</tr>
<tr>
<td>Overall mean displacement</td>
<td>34.12</td>
<td>44.16</td>
</tr>
</tbody>
</table>

* Results expressed in millimetres (mm)
2.3 Pilot 2

Since the array had only been piloted on 3 participants, setting a learning criterion was problematic. The participants in the second pilot completed all other assessments described below, thus fatigue played a role in their ability to endure successive learning trials. Of 6 participants (3 male, 3 female) with a mean age of 9.75 years (S.D. = 0.3; range 9.5–10), 1 participant received 6 learning trials, 2 received 7 and 3 received 8 learning trials. Following analysis of their scores across learning trials and at the 30 minute and 1 week delays according to the maximum radius measurement (see Table 2), it was evident that participants were remembering the object-locations. However, participants often obtained their highest score within the first 5 trials and so some degree of over-learning was probably occurring. At this point, the learning criterion underwent a further modification. Participants would be given a minimum of 2 and a maximum of 10 consecutive trials to make 7 object placements to within the 34mm radius. Displacement scores would be calculated for immediate recall, recall at the last learning trial, at 30 minutes and at 1 week.

**Figure 2.** The stencil used during learning trials to determine whether participants had placed objects within the maximum radius of 34mm.
Table 2.
Pilot 2 scores across learning trials (placements within 34mm maximum radius)

<table>
<thead>
<tr>
<th>Trials</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>30mins</th>
<th>1 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant 1</td>
<td>80*</td>
<td>100</td>
<td>70</td>
<td>90</td>
<td>70</td>
<td>90</td>
<td></td>
<td>90</td>
<td></td>
<td>40</td>
</tr>
<tr>
<td>Participant 2</td>
<td>70</td>
<td>70</td>
<td>60</td>
<td>80</td>
<td>60</td>
<td>50</td>
<td>50</td>
<td>60</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Participant 3</td>
<td>50</td>
<td>40</td>
<td>70</td>
<td>60</td>
<td>70</td>
<td>80</td>
<td>90</td>
<td>70</td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>Participant 4</td>
<td>30</td>
<td>60</td>
<td>80</td>
<td>100</td>
<td>90</td>
<td>100</td>
<td>90</td>
<td>90</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Participant 5</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>60</td>
<td>90</td>
<td>50</td>
<td>70</td>
<td>60</td>
<td>70</td>
<td>50</td>
</tr>
<tr>
<td>Participant 6</td>
<td>90</td>
<td>70</td>
<td>70</td>
<td>70</td>
<td>90</td>
<td>80</td>
<td>60</td>
<td>80</td>
<td>80</td>
<td></td>
</tr>
</tbody>
</table>

* Results expressed as %

2.4 Main Study

Power. Power was calculated using 1-week recall data from Davidson et al.’s (2007) study, since the same standardised measure of verbal memory was used here and memory was assessed after delays of equivalent length with a sample of same-aged children with and without a diagnosis of IGE. Assuming normal distribution, equal variance between groups and a significance level of 0.05, it was calculated that 21 participants were required for each group to achieve a power of 0.79.

Few published studies have explored the spatial abilities of children with epilepsy which was partly a reason for incorporating a new spatial object-locations task in the present study. Volkl-Kernstock et al. (2006) designed a study to investigate spatial perception and memory in children with BCECTS compared to healthy controls. In a task that required participants to remember figures built from cubes and to rebuild them or memorise them over multiple trials, children with BCECTS exhibited spatial memory impairments. This task shares some similarities with the current spatial object-locations task because participants were required to memorise the locations of objects within in a spatial arrangement and recreate it over 3 trials. Using their immediate recall data (because participants were not tested after extended delays), assuming normal distribution, equal variance between groups and a significance level of 0.05, 8 participants were required for each group to achieve a power of 0.8.

Participants.

Idiopathic generalised epilepsy participants. Nine children aged between 10 and 16 years with an established diagnosis of IGE were recruited from the epilepsy clinic at The Royal Hospital for Sick Children in Edinburgh. Testing took place on the neurology ward. Medical records were examined by the treating consultant paediatric
neurologist to determine suitability for inclusion, as specified below. A further 2 children, aged 7 and 12, were recruited via an epilepsy charity based in Livingston, West Lothian. Informed consent was always sought from both the child and a parent or guardian and an assent form was completed by participants at the time of data collection. No patient had a history of developmental delay, a Full Scale IQ of less than 70, a history of head injury or any diagnosed medical conditions or neurological disorder other than IGE. This was to ensure that any memory impairments found could not be attributed to other clinical conditions. Due to the nature of the assessment materials, children who did not understand verbal explanations or written English were excluded. Of the 11 patients recruited, 5 were not available to be tested during the study period and 1 dropped out after the 1st session. The remaining 5 (2 male, 3 female) had a mean age of 11.30 (S.D. = 2.88; range 7–14.5). All IGE group participants were receiving anti-epileptic medication. The clinical characteristics of the IGE group were provided by the treating consultant paediatric neurologist and are summarized in Table 3.

<table>
<thead>
<tr>
<th>Syndromal diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood absence epilepsy</td>
<td>0</td>
</tr>
<tr>
<td>Juvenile absence epilepsy</td>
<td>4</td>
</tr>
<tr>
<td>Juvenile myclonic epilepsy</td>
<td>0</td>
</tr>
<tr>
<td>Generalised tonic-clonic seizures only</td>
<td>1</td>
</tr>
<tr>
<td>Unclassified epilepsy</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epilepsy status</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>5</td>
</tr>
<tr>
<td>Remitted</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current seizure frequency</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>None in last 2 years (remitted)</td>
<td>0</td>
</tr>
<tr>
<td>Daily</td>
<td>0</td>
</tr>
<tr>
<td>1 or 2 per week</td>
<td>1</td>
</tr>
<tr>
<td>1 or 2 per month</td>
<td>2</td>
</tr>
<tr>
<td>Less than 1 per month</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Current number of antiepileptic drugs</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antiepileptic drugs prescribed</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamotrigine</td>
<td>3</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>1</td>
</tr>
<tr>
<td>Keppra oral solution</td>
<td>1</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
</tbody>
</table>

* Result expressed an n
Healthy control participants. All controls were recruited from primary and secondary schools in Edinburgh and also via an email sent to university staff. Children were either tested at their school or they came to the university psychology department. The exclusion criteria were the same as that applied to the IGE group to ensure that the control group’s performance was not influenced by conditions which might be expected to negatively impact on memory functioning. Additionally, control participants were excluded if they had a family history of epilepsy. IGE and control group participants were matched as closely as possible for age and IQ. Thirteen controls (7 male, 6 female) with a mean age of 10.81 (S.D. = 1.70; range 9–15) completed the standard assessment and stories and dot locations subtests. Of these, 7 (4 male, 3 female) completed the spatial object-locations task (mean age = 11.71; SD = 1.91).

Standard assessment.

The Wechsler Intelligence Scale for Children - Fourth UK Edition (WISC-IV UK). The WISC-IV (Wechsler, 2004) provides a measure of children’s intellectual ability and is one of the most popular standardised assessments of its kind. Its 10 core subtests which produce 4 composite scores in verbal comprehension (VCI), perceptual reasoning (PRI), processing speed (PSI) and working memory (WMI), were administered to generate a Full Scale score (FSIQ) for each participant.

Memory and educational progress of IGE participants. Information regarding the IGE group’s memory problems and educational progress was collected from parents and guardians via a brief questionnaire (see Appendix E). Participants in the IGE group were asked to rate their experience of functional memory difficulties according to the same scale used in question 1 of this questionnaire.

Experimental assessment. To assess participant’s memory, a verbal and a visuo-spatial subtest from the Children’s Memory Scale (CMS) (Cohen, 1997) and a new spatial object-locations task were administered.

‘Stories’ subtest. In accordance with the standard administration procedure, 1 of 3 versions of the stories subtest was used depending on participants’ age. Participants were read aloud 2 short stories and required to learn them to 90% accuracy over a minimum of 2 consecutive trials. During recall, participants attempted to repeat the story they had heard verbatim. For the recognition component at 30 minutes and 1 week, participants were asked to give a yes or no response to 15 questions about each story.
‘Dot Locations’ subtest. In accordance with the standard administration procedure, 1 of 2 versions of the dot locations subtest was used depending on participants’ age. Participants were shown 8 counters on a grid and required to learn their positions. As for the verbal subtest, they were given a minimum of 2 and a maximum of 10 consecutive trails to learn the positions of the counters to 83% accuracy; the 2 age versions of the dot locations derived different total scores. Participants were required to place the counters into their designated positions in the grid and the learning criterion allowed for 1 incorrectly placed counter.

Spatial object-locations task. This task is described above, in the descriptions of the pilot studies. During recall of object-locations, participants were given a minimum of 2 and maximum of 10 consecutive trials to place 7 of the 10 toy objects within a 34mm radius of the correct location shown in the original array. This criterion ensured that participants had learnt the approximate positions for the majority of toy objects, but their displacement scores were used to compare patients and controls.

Procedure. Recall was performed immediately and repeated after delays of 30 minutes and 1 week, the recognition component of the stories subtest was performed at 30 minutes and 1 week. Each participant was met on 3 separate occasions to prevent interference occurring between the 2 non-verbal tasks, which both required participants to learn the positions of objects (see Table 4 for protocol).

During the first testing session, the dot locations and stories subtests were administered according to the procedure outlined in the CMS manual. Participants who did not reach the learning criterion within a maximum of 10 trials were excluded further from the study. After the last learning trial, the 30 minute interval was used to complete some of the WISC subtests; those that were not visuo-spatial or verbal in nature. Finally, delayed recall of dot locations and delayed recall and recognition of stories was assessed at 30 minutes. At the end of the session, participants were told that they would be asked to complete similar types of tasks at our next meeting. They were not explicitly told not to rehearse the material, but they were given no reason to think that their memory for the tasks they had completed so far would be re-tested.

Exactly 1 week later, recall and recognition (stories subtest only) memory for the dot locations and stories material was re-tested. The spatial object-locations task was administered and again, those who did not reach the learning criterion were excluded further from the study. The predominantly verbal subtests from the WISC
were completed during the 30 minute interval prior to delayed recall of the toy positions from the spatial object-locations task.

After a further 1 week interval, the recall component of the spatial object-locations task was repeated. The remaining uncompleted WISC subtests were administered at this point. Finally, participants with IGE and their accompanying parent or guardian provided their ratings of memory and educational progress. It should be noted that prior to each testing session, children from this group and their carers were asked if they had experienced a seizure since the previous testing session and whether there had been any changes to their medication.

**Statistical Analysis.** All statistical analyses were carried out using PASW Statistics 17.0 for Windows. Data were analysed using mixed analysis of variance (ANOVA), with a within-participants factor of delay (30 minutes vs. 1 week) and a between-participants factor of group (IGE vs. control). Planned comparisons were conducted using independent *t* tests or Mann-Whitney *U* tests as appropriate. Significance levels were set at ≤ 0.05.

### Table 4.
**Testing protocol of experimental assessments and WISC subtests**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Dot locations (immediate recall, learning trials)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stories (immediate recall, learning trials)</td>
</tr>
<tr>
<td></td>
<td>Digit span</td>
</tr>
<tr>
<td></td>
<td>Picture concepts</td>
</tr>
<tr>
<td></td>
<td>Coding</td>
</tr>
<tr>
<td></td>
<td>Symbol search</td>
</tr>
<tr>
<td></td>
<td>Dot locations (30 min recall)</td>
</tr>
<tr>
<td></td>
<td>Stories (30 min recall and recognition)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week 2</th>
<th>Dot locations (1 week recall)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stories (1 week recall and recognition)</td>
</tr>
<tr>
<td></td>
<td>Spatial object-locations (immediate recall, learning trials)</td>
</tr>
<tr>
<td></td>
<td>Similarities</td>
</tr>
<tr>
<td></td>
<td>Vocabulary</td>
</tr>
<tr>
<td></td>
<td>Comprehension</td>
</tr>
<tr>
<td></td>
<td>Spatial object-locations (30 min recall)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week 3</th>
<th>Spatial object-locations (1 week recall)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Block design</td>
</tr>
<tr>
<td></td>
<td>Letter-number sequencing</td>
</tr>
<tr>
<td></td>
<td>Matrix reasoning</td>
</tr>
</tbody>
</table>
3. Results

3.1 Memory and Educational Progress of IGE Participants

IGE participants and their parents’ ratings of memory functioning and educational progress are presented in Table 5. Just 2 children reported experiencing memory problems, whilst the majority of parents reported the presence of memory problems and tended to rate them as more problematic. Interestingly, the parent of 1 child reporting no difficulties rated their child’s memory problems as ‘quite problematic’. All participants were at mainstream schools, with 2 having received learning support at some time. Of 3 parents showing concern about their child’s school progress, only 1 child had ever received learning support. None had repeated a school year. There were no instances of IGE participants or parents rating memory problems or school concerns at the most severe end of the scale.

Table 5.
Memory and educational progress ratings for IGE group (n=5)

<table>
<thead>
<tr>
<th>Child ratings of memory problems</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No problems</td>
<td>3*</td>
</tr>
<tr>
<td>A little problematic</td>
<td>1</td>
</tr>
<tr>
<td>Quite problematic</td>
<td>1</td>
</tr>
<tr>
<td>Very problematic</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parent ratings of child’s memory problems</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No problems</td>
<td>1</td>
</tr>
<tr>
<td>A little problematic</td>
<td>2</td>
</tr>
<tr>
<td>Quite problematic</td>
<td>2</td>
</tr>
<tr>
<td>Very problematic</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Repeated school year</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
<td>No</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ever received learning support</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parent rating of school progress</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No problems</td>
<td>2</td>
</tr>
<tr>
<td>Mildly concerned</td>
<td>1</td>
</tr>
<tr>
<td>Quite concerned</td>
<td>2</td>
</tr>
<tr>
<td>Very concerned</td>
<td>0</td>
</tr>
</tbody>
</table>

* Result expressed an n
3.2 Experimental Assessment of Very Long-Term Memory

There were 5 participants with IGE and 13 controls included in the analyses. Results of an independent \( t \) test shown in Table 6 revealed no significant differences between the groups in terms of age or full scale IQ.

| Participants’ mean age and IQ and results of independent samples \( t \) test |
|--------------------------|-----------------|--------|-----|
|                          | IGE             | Controls | \( t \) (16) | \( P \) |
| Age (SD)                 | 11.30 (2.88)    | 10.81 (1.70) | 0.45 | 0.66 |
| Full scale IQ (SD)       | 96.40 (13.35)   | 99.38 (12.08) | -0.46 | 0.65 |

**Stories subtest.** Descriptive statistics for performance on the stories subtest are presented in Table 7. Recall scores were converted into percentages because the 3 age-appropriate versions of the stories subtest produced different total scores. Raw scores were used for analysis of recognition performance because in all versions there was a maximum total score of 30.

**Table 7.** Descriptive statistics for performance on the stories subtest

<table>
<thead>
<tr>
<th></th>
<th>IGE</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD)</strong></td>
<td><strong>Range</strong></td>
<td><strong>Mean (SD)</strong></td>
</tr>
<tr>
<td>Immediate recall(%)</td>
<td>63.90 (20.29)</td>
<td>38-88</td>
</tr>
<tr>
<td>Trials to criterion(( n ))</td>
<td>4.1 (2.10)</td>
<td>2-7.5</td>
</tr>
<tr>
<td>Criterion recall(%)</td>
<td>93.30 (3.09)</td>
<td>90-97.5</td>
</tr>
<tr>
<td>30 mins recall(%)</td>
<td>79.90 (12.27)</td>
<td>61.5-95</td>
</tr>
<tr>
<td>1 week recall(%)</td>
<td>67.30 (16.72)</td>
<td>47.5-90</td>
</tr>
<tr>
<td>30 mins recognition</td>
<td>27.00 (3.54)</td>
<td>21-30</td>
</tr>
<tr>
<td>1 week recognition</td>
<td>26.80 (2.86)</td>
<td>22-29</td>
</tr>
</tbody>
</table>

Trials to criterion(\( n \)) = The average number of trials taken to reach the learning criterion for each story. Criterion recall(%) = Percentage of stories recalled at the last learning trial.

A 1-sample Kolmogorov-Smirnov test of goodness-of-fit was not significant, confirming that IGE and control group data was normally distributed (see Table 8).

Independent \( t \) tests revealed no significant difference between the number of learning trials IGE participants and controls required to reach criterion (\( t \) (4.22) = 1.64; \( p = 0.17 \)). There were no significant differences between groups with regards to percentage of stories recalled immediately (\( t \) (16) = -1.35; \( p = 0.19 \)) or percentage recall at 30 minutes (\( t \) (4.40) = -1.79; \( p = 0.14 \)). Group differences in percentage recall
at 1 week approached significance ($t(4.22) = -2.29; p = 0.08$) indicating a strong trend for poorer recall of the IGE group following a 1 week delay. Analysis of the recognition data revealed no group differences in scores at 30 minutes ($t(4.18) = -0.43; p = 0.69$) or at 1 week ($t(16) = -1.10; p = 0.29$).

**Table 8.**

<table>
<thead>
<tr>
<th></th>
<th>Absolute value of largest difference (D)</th>
<th>Exact $P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGE</td>
<td>Controls</td>
</tr>
<tr>
<td>Immediate recall</td>
<td>0.16</td>
<td>0.16</td>
</tr>
<tr>
<td>30 minutes recall</td>
<td>0.21</td>
<td>0.17</td>
</tr>
<tr>
<td>1 week recall</td>
<td>0.22</td>
<td>0.13</td>
</tr>
<tr>
<td>30 mins recognition</td>
<td>0.30</td>
<td>0.26</td>
</tr>
<tr>
<td>1 week recognition</td>
<td>0.33</td>
<td>0.28</td>
</tr>
</tbody>
</table>

A repeated measures ANOVA was applied to investigate the effects of delay on participants’ percentage story recall. There were significant main effects of group ($F(1) = 12.03; p = < 0.01$) delay ($F(2) = 39.42; p = < 0.01$) and a significant group x delay interaction ($F(2) = 7.59; p = < 0.01$). Data are presented in Figure 3 which illustrates that the IGE group forgot the stories material at a steeper rate than controls. Confidence intervals are stable for controls but those of the IGE group become very large at 30 minute and 1 week recall. The percentage recall scores of 1 IGE participant were much lower than the group mean and she obtained the lowest recall scores at both 30 minutes and 1 week. This participant was 7 years old and the youngest IGE participant in the study, however all participants completed age-appropriate versions of the stories subtest and so her data was included in all analyses. The effect of removing her data on the IGE group’s rate of forgetting is shown in Figure 4.

**Dot locations subtest.** Descriptive statistics for performance on the dot locations subtest are summarised in Table 9. Recall scores were converted into percentages because the 2 age-appropriate versions of the dot locations subtest produced different total scores.

A 1-sample Kolmogorov-Smirnov test of goodness-of-fit was not significant, confirming that control and IGE data was normally distributed (see Table 10).
Independent $t$ tests revealed no significant differences between IGE participants and controls with respect to the number of learning trials required to reach criterion ($t (4.30) = 0.79; p = 0.47$). No significant group differences were found for percentage of dot locations recalled immediately ($t (4.99) = -0.72; p = 0.50$), percentage recall at 30 minutes ($t (10.95) = 1.25; p = 0.24$) or percentage recall at 1 week ($t (5.89) = 0.10; p = 0.92$).

A repeated measures ANOVA was applied to investigate the effects of delay on participants’ percentage recall of the dot-locations. Mauchley’s Test of Sphericity indicated that there was heterogeneity of variance. The more conservative Greenhouse-Geisser test indicated a significant effect of delay ($F (1.16, 18.62) = 5.87; p = 0.02$). There was no significant effect of group ($F (1) = 0.23; p = 0.64$), nor was there a significant group x delay interaction ($F (2) = 0.06; p = 0.85$). Data are illustrated in Figure 5. Rates of forgetting are equivalent between groups. Confidence intervals become larger for both groups across the delays, noticeably so for the IGE group.
Figure 4. Graph of stories mean recall scores (%) for the IGE and control groups at criterion, and after 30 minute and 1 week delays. Data of youngest and poorest scoring IGE participant removed.

Table 9. Descriptive statistics for performance on the dot locations subtest

<table>
<thead>
<tr>
<th></th>
<th>IGE</th>
<th></th>
<th>Controls</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate recall (%)</td>
<td>83.33 (17.92)</td>
<td>63-100</td>
<td>89.42 (10.01)</td>
<td>75-100</td>
</tr>
<tr>
<td>Trials to criterion(n)</td>
<td>2.40 (0.89)</td>
<td>2-4</td>
<td>2.08 (0.28)</td>
<td>2-3</td>
</tr>
<tr>
<td>Criterion recall(%)</td>
<td>100 (0.00)</td>
<td></td>
<td>98.08 (4.69)</td>
<td>88-100</td>
</tr>
<tr>
<td>30 mins(%)</td>
<td>97.50 (5.59)</td>
<td>88-100</td>
<td>93.27 (8.25)</td>
<td>75-100</td>
</tr>
<tr>
<td>1 week(%)</td>
<td>85.00 (27.01)</td>
<td>38-100</td>
<td>83.65 (20.66)</td>
<td>50-100</td>
</tr>
</tbody>
</table>

Table 10. Normality of distribution of data from the dot locations subtest

<table>
<thead>
<tr>
<th></th>
<th>Absolute value of largest difference (D)</th>
<th>Exact P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGE</td>
<td>Controls</td>
</tr>
<tr>
<td>Immediate recall</td>
<td>0.22</td>
<td>0.24</td>
</tr>
<tr>
<td>30 mins recall</td>
<td>0.47</td>
<td>0.33</td>
</tr>
<tr>
<td>1 week recall</td>
<td>0.34</td>
<td>0.27</td>
</tr>
</tbody>
</table>
Spatial object-locations task. It was intended that very long-term memory would be assessed after a delay of 1 week, however it was not always possible to see participants exactly 7 days after their previous testing session. Of 7 controls who completed the spatial object-locations task, 3 performed recall at an extended delay of 2 weeks. Mann-Whitney U tests revealed no significant difference between the mean object-displacement scores of controls who performed recall at 1 week and 2 weeks ($U = 2.00$; exact $p = 0.23$), subsequently all 7 controls were included in the analysis. For the purpose of reporting the data, very long-term recall was labelled as 1 week recall. Results of an independent $t$ test shown in Table 11 revealed no significant differences between IGE and controls group participants in terms of age or full scale IQ.

Descriptive statistics for performance on the spatial object-locations ask are given in Table 12
Table 11.
Participants’ mean age and IQ and results of independent samples t test

<table>
<thead>
<tr>
<th></th>
<th>IGE</th>
<th>Controls</th>
<th>t(10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>11.30 (2.88)</td>
<td>11.71(1.91)</td>
<td>-0.30</td>
<td>0.77</td>
</tr>
<tr>
<td>Full scale IQ (SD)</td>
<td>96.40(13.35)</td>
<td>94.86(8.13)</td>
<td>0.25</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Table 12.
Descriptive statistics for performance on the spatial object-locations task

<table>
<thead>
<tr>
<th></th>
<th>IGE Mean displacement (SD)</th>
<th>Controls Mean displacement (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate recall (mm)</td>
<td>67.38 (25.89)</td>
<td>58.69 (19.15)</td>
</tr>
<tr>
<td>Trials to criterion (n)</td>
<td>4.20 (1.64)</td>
<td>3.43 (1.62)</td>
</tr>
<tr>
<td>Criterion recall (mm)</td>
<td>31.10 (2.68)</td>
<td>34.17 (9.06)</td>
</tr>
<tr>
<td>30 mins (mm)</td>
<td>33.56 (4.62)</td>
<td>40.74 (13.05)</td>
</tr>
<tr>
<td>1 week (mm)</td>
<td>60.52 (22.82)</td>
<td>58.96 (39.10)</td>
</tr>
</tbody>
</table>

A 1-sample Kolmogorov-Smirnov test of goodness-of-fit was not significant, confirming that participants’ data was normally distributed (see Table 13).

Table 13.
Normality of distribution of data from the spatial object-locations task

<table>
<thead>
<tr>
<th></th>
<th>Absolute value of largest difference (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IGE Controls IGE Controls</td>
</tr>
<tr>
<td>Immediate recall</td>
<td>0.25 0.32</td>
</tr>
<tr>
<td>30 mins recall</td>
<td>0.25 0.18</td>
</tr>
<tr>
<td>1 week recall</td>
<td>0.24 0.32</td>
</tr>
</tbody>
</table>

Independent samples t tests did not indicate a difference in the number of learning trials that IGE participants and controls required to reach criterion (t(10) = 0.81; p = 0.44). Nor were there group differences between mean displacements scores at either immediate recall (t(10) = 0.67; p = 0.52), 30 minutes (t(10) = -1.17; p = 0.27) or 1 week (t(10) = 0.08; p = 0.94).

A repeated measures ANOVA was applied to investigate the effects of delay on participants’ mean displacement scores. Mauchley’s Test of Sphericity indicated that there was heterogeneity of variance. The more conservative Greenhouse-Geisser test indicated a significant effect of delay (F(1.17, 11.75) = 4.97; p = 0.02). There was no significant effect of group (F(1) = 0.25; p = 0.63), nor was there a significant group x delay interaction (F(1.17) = 0.11; p = 0.78). Groups’ pattern of recall performance is demonstrated in Figure 6. Mean displacement scores become larger.
and thus less accurate across the delays. Confidence intervals for both groups become very large at 1 week recall.

**Figure 6.** Graph of mean displacement scores (mm) for the IGE and control groups at criterion and after 30 minute and 1 week delays.
4. Discussion

4.1 Findings and Implications

The current study aimed to further explore memory and forgetting in children with idiopathic generalised epilepsy (IGE) in comparison to a healthy group of controls who did not differ in age or IQ. Accelerated long-term forgetting (ALF) was investigated by assessing memory over an extended retention period, beyond those measured by standardised tests. Simultaneously, a new non-verbal memory measure in the form of a spatial object-locations task was developed and its sensitivity to ALF was evaluated. Guided by prior research, it was hypothesised that immediate recall and recall at 30 minutes would be comparable across groups, but IGE participants would forget material at an accelerated rate and recall significantly less than controls at 1 week. This effect however, would be mediated by the poorer learning efficiency of children with IGE as demonstrated by their need for significantly more learning trials to reach criterion. An alternative hypothesis proposed that if participants were indistinguishable in terms of the number of learning trials taken, ALF might be due to a failure to consolidate memories effectively - in which case recognition memory would be impaired, or due to difficulties retrieving information from memory - in which case recognition memory would remain intact.

Results indicated that as hypothesised, participants displayed equivalent recall of verbal material from the stories subtest when memory was tested immediately and after a standard delay of 30 minutes. Group differences in recall performance that were approaching significance emerged at the extended 1-week delay, at which there was a strong trend for IGE participants to recall less than controls. A significant main effect of group and delay further supported the assertion that the forgetting rate of children with IGE follows a different trajectory to that of healthy controls because the IGE group forgot information at a faster rate over time. Inspection of the mean scores revealed a substantial difference in the percentage of stories material retained by IGE and control group participants at 1 week. Such a difference in scores would be expected to reach significance in a larger sample. In accordance with the alternative hypothesis, groups did not differ in the number of trials required to reach the learning criterion, therefore this could not be mediating the effect of the poorer very-long term recall shown by the IGE group. Consideration of the mean scores raises the possibility
that group differences in the number of learning trials might have obtained significance in a larger sample, however 1 IGE participant who required 7 trials to reach criterion for story A and 8 for story B was driving this higher mean score. The pattern of forgetting demonstrated by children with IGE at 1 week recall was not replicated in their recognition performance. When recognition memory for the stories was tested at 30 minutes and after 1 week, IGE participants and controls achieved equivalent scores, confirming that the verbal material had been successfully consolidated and stored in long-term memory. Therefore, during free recall at very long-term delays only, the poorer performance of children with IGE was due to difficulties accessing and retrieving material from memory. Such retrieval difficulties were not apparent when memory was tested at standard delays because recall memory of the IGE group was intact at 30 minutes.

Non-verbal memory was not vulnerable to ALF since the analyses found no significant differences between IGE and control groups’ percentage recall of dot locations or object-locations at any of the delays. This is contrary to previous research by Jambaque et al. (1993) who found that children with IGE were selectively impaired on a range of non-verbal memory measures, although tasks used were visual rather than spatial. Elsewhere, Nolan et al.’s (2004) sample included children with childhood absence epilepsy (CAE) (an IGE syndrome) who showed very mild general impairment but a significant visuo-spatial memory deficit. Neither of these studies identified any verbal memory impairment. Analyses also indicated that there were no group differences in the number of trials required to reach the learning criterion on the dot locations or object-locations tasks, indicating that all participants learnt and subsequently forgot non-verbal information at a comparable rate. Inspection of the means suggested that the spatial object-locations task may be a more sensitive measure of ALF. All participants performed exceptionally well on the dot locations subtest and memory declined only slightly over the delay period. The grid system, in which there were 16 possible locations for 8 counters, enabled participants to make informed guesses if they were uncertain about the final placement, whereas during the object-locations task the only available cues were the positions of toys that had already been recalled. An interesting observation noted during data collection was that participating children frequently commented on the simplicity of the dot locations subtest. Recall accuracy on the object-locations task, as measured by the distance between participants placements made during recall and the objects’ designated
positions in the original array, deteriorated at an expected rate; displacement scores were not stable across the delay period which might have indicated an over-simplistic task, neither were they too large to suggest that participants were making random placements of the toy objects during recall. The data provide preliminary support for utilising the object-locations task as a measure of non-verbal memory that is sensitive to rates of forgetting of spatial information.

Corroborating previous research (Davidson et al., 2007) the current study supports the incidence of ALF of verbal material in children with IGE. Conversely, a lack of group differences in learning efficiency is not consistent with Davidson et al.’s (2007) finding that poorer recall at longer delays was attributable to the greater number of learning trials required by their IGE sample to reach criterion level. The fact that a strong trend for ALF was manifest despite all participants showing normal learning is consistent with investigations of memory in adults with epilepsy, in whom ALF is a disorder of memory consolidation (Blake et al., 2000). If this is the case, children with IGE were unable to perform more extensive, long-term consolidation of the acquired verbal material which impaired recall at 1 week. Consolidation theories posit that the hippocampal system facilitates memory traces to become more stable via the formation of and increased activity among neocortical connections. According to Squire (1997), memories are eventually stored independently of the hippocampus, whilst Nadel and Moscovitch (1997) maintain that the creation of distributed memory traces always originate in the hippocampus. Determining how processes responsible for memory consolidation are disrupted in an epilepsy population with no structural damage, may be explained in terms of epileptiform activity preventing connections between cortical regions being generated. In those with reasonably low seizure frequency - the majority of IGE participants were experiencing less than 1 seizure per month or between 1 and 2 per month, subclinical epileptic discharges may be culpable (Zeman, 2009). If epileptiform activity is responsible for poorer memory in people with epilepsy, the possibility that it erases successfully consolidated memories, rather than preventing or disrupting such processes, cannot be ruled out.

Although ALF is thought to provide evidence that unsuccessfully consolidated memories are lost and have not reached permanent storage, the failed consolidation hypothesis does not completely tie in with the current data. If the IGE group are rapidly forgetting stories material over the long-term, some impairment in recognition
performance might be expected. The most convincing evidence of ALF in the epilepsy literature has demonstrated that recognition memory is also significantly impaired in epilepsy populations relative to healthy controls (Butler et al., 2010). In the present study, children with IGE maintained their ability to discriminate between correct and incorrect statements about the stories at all delays. Crucially at 1 week, when they were unable to recall the material that had been successfully recalled at a shorter time interval, recognition performance suffered no deterioration whatsoever. Intact recognition disputes the premise that memories did not undergo long-term consolidation between 30 minutes and 1 week. Alternatively, the failed consolidation account may prevail if it is assumed that more thorough and extensive consolidation processes must be applied to material to ensure effective long-term recall, but that these processes are not essential for recognition. Poorer quality memory traces may be sufficient for recall at 30 minutes but with increasing time the threshold for retrieval failure may be met sooner than for better quality traces. The memory processes operating between initial learning and standard delays, and even perhaps during the learning trials, might constitute a less robust form of consolidation, which was adequate for subsequent cued retrieval of previously learnt information. Effective long-term recall however, may be dependent on a more gradual, multiple-staged consolidation process. Very long-term consolidation that strengthens memory traces and makes memories more resistant to decay and forgetting may not be as efficient in children with IGE as it is in healthy controls, resulting in poorer recall following a 1-week delay. Adopting Tulving’s (1974) stance, the finding of impaired retrieval in conjunction with intact recognition does not necessarily need to be reconciled if forgetting is considered in the context of retrieval failure. In this sense, children with IGE appear prone to ALF of verbal material which would not be automatically assumed to affect recognition performance if the appropriate cues were provided for recall.

If the current findings are interpreted as a retrieval deficit rather than a memory problem per se, then consideration of impairment in other areas of cognition such as executive functioning (EF) is appropriate in children with IGE. This would not be new; executive dysfunction in IGE has received attention in the literature (Hommet et al., 2006). Dissociation between recall and recognition memory performance could indicate that all participants learnt and consolidated verbal
material normally but when memory was tested at the long-term delay, those with IGE faced significant difficulties initiating strategies to access and retrieve successfully stored information. Successful recall involves complex, higher-level cognitive processes. The recognition questions and possible responses from the stories subtest provided participants with cues to stimulate retrieval processes and reduced the demands of searching for information acquired in the past. However, the absence of a group difference in percentage recall at shorter delays renders an executive dysfunction hypothesis less convincing. It is not clear how IGE participants were capable of retrieving the stories at 30 minutes or why retrieval difficulties only surfaced when recall memory was tested the following week. One explanation might be that retrieval at 30 minutes, a relatively short interval after learning to criterion, is qualitatively different to retrieval after extended periods during which material is not rehearsed. At 30 minutes, recency effects may also be playing a part and aiding recall. Deficits in EFs offer a partial account for impaired recall versus intact recognition, nevertheless analyses revealed a significant delay and group interaction, indicating that the IGE group’s rate of forgetting was different to that of controls. This finding is not easily explained solely in terms of executive dysfunction, though the combination of subtle executive deficits in addition to memory impairments may occur in this population.

All but 1 of the IGE participants in this study were receiving anti-epileptic drug (AED) treatment and this must be considered as a potential contributory factor to poorer verbal memory performance. In children with epilepsy especially, AEDs may have adverse effects on cognitive development and learning (Bourgeois, 2004). Moreover, the impact of medication is likely to vary depending on children’s ages. The 7-year-old in the current sample was not medicated, but the effects of AEDs on the cognitive functioning of the 10-year-old participant may differ to that of the 14-year-old for example, because of the different developmental stages at which they are at. Additional factors such as the age at which medication was initiated and how long it has been prescribed are also relevant, but were not considered in the present study. Interestingly, the 1 IGE participant to rate their memory problems as ‘quite problematic’ was the only participant receiving polytherapy; their parents were also ‘quite concerned’ about their child’s memory and school progress. Newer AEDs are reported to have minimal detrimental effects (Lagae, 2006) and Aldenkamp et al.
(2002) found no significant differences in memory performance between healthy participants taking sodium valproate, lamotrigine or a placebo. Unavoidably, epilepsy research is complicated by the type and number of AEDs prescribed to participants. The presence of memory problems in less medicated populations, such as those with IGE, enables more meaningful associations to be made between the epilepsy disorder itself and impairment.

4.2 Limitations and Future Directions

A clear shortcoming of the current research is the small sample size, particularly the number of participants in the IGE group. As a result, it was not possible to achieve the intended power levels that were calculated prior to data collection, thus drawing conclusions from the analyses must be approached with caution. The current study was exploratory in nature, incorporating the development of a new spatial, non-verbal memory measure and the findings warrant further investigation in larger samples. Moreover, the fact that performance of the IGE group did not exactly replicate what previous work with children with IGE has shown (Davidson et al., 2007) also advises further research of ALF in this clinical group to clarify the causes of their poorer long-term recall.

Piloting of the object-locations task as well as its administration in the main study highlighted several limitations to be addressed in future. In order to derive the learning criterion, mean displacement scores of the 10 toy objects were calculated for each participant and this was then averaged to produce 1 score representing their mean displacement for the whole array. Finally, a group mean displacement score was calculated, providing a general indication of how far participants were placing objects away from their designated position in the original array. Although this was a rational way to obtain a learning criterion, data was obtained from only 3 participants and it would be false to assume that a wider population of children would perform equivalently. It is likely that the learning criterion used in the current study would be subject to modification if the pilot were to be replicated in a larger sample with greater variation in age. Nonetheless, all participants were able to reach the criterion and place 7 of the 10 toys objects no further than 34mm away from their correct position within 10 learning trials; the majority did so within 5 trials.
Observing participants’ performance on this task it was noted that occasionally, the wrong toy object would be placed in the correct location of another object. In such cases, the participant had recalled a genuine spatial location, but had not made the correct object-location association. Because displacement measurements were used to determine how well participants remembered the array, displacement scores for objects placed in the locations of other objects were very large and thus had a substantial, negative effect on the overall mean displacement score. However, the task was presented as a measure of memory for objects in space that requires participants to encode and retrieve object-location associations. It might be of interest to remove the object element of the task and use identical objects such as the counters used in the dot locations subtest. This would require participants to encode spatial locations only and consequently, object displacement scores might be a more accurate reflection of participants’ memory for the visual array. The absence of nameable objects may also have a negative impact on recall performance, especially when the task is being used with children. Without any distinguishable objects such as toys, the object-familiarisation stage would become impossible and encouraging participants to remember the positions of counters would be much more difficult. Further piloting of the spatial object-locations task might investigate these issues.

In the current study there was a strong trend for children with IGE to recall less of the stories material than controls at a delay of 1 week, which in Davidson et al.’s (2007) study achieved significance. To date, ALF in children with IGE appears to be material-specific which must be a focus of subsequent research. There is no seizure focus in IGE syndromes and epileptic activity is generalised across both hemispheres, therefore further investigation of the isolated effect of ALF for verbal memory is needed. Using different types of verbal material might provide further insight into the mechanisms producing ALF. Isaac and Mayes (1999a) found accelerated forgetting of prose in amnesic patients over delays of up to 10 minutes, whereas memory for semantically unrelated word-lists declined at a normal rate (Isaac & Mayes, 1999b). The authors suggested that dissociable forgetting rates of semantically related and unrelated material was due to the additional processing demands of consolidating information organised by multiple, complex associations. Their hypothesis was strengthened by the fact that amnesics’ recognition memory was intact. As discussed above, during recognition it is not necessary to initiate strategies
that enable the retrieval of meaningfully connected information; the presentation of possible responses cues these processes. These findings may be relevant to samples of children with IGE, who in the current study, were impaired during recall after a very long-term delay but performed recognition similarly to controls. At the very least, finding no evidence of ALF for semantically unrelated material would add weight to the interpretation that EFs in those with IGE are not operating as well as in healthy controls. More general assessment of executive functioning in IGE might also be pursued in future.

Despite much attention being paid to the comparable recognition memory of IGE participants and controls, potential problems with the recognition task itself must be evaluated. Though the stories subtest is a well-normed, standardised measure, participants performed close to ceiling level and mean recognition scores were almost identical between groups. One IGE participant obtained the poorest recognition scores when tested at both 30 minutes and 1 week and this child’s scores were much lower than the group mean, but all other participants achieved scores of 26 out of 30 or above. The median recognition score for IGE and control group participants at 30 minutes and 1 week was 28 out of 30. Such reduced variance in scores risks the possibility that the recognition component of the stories subtest was too easy and thus insensitive to any group differences in recognition memory. As suggested above, investigating recognition memory using other verbal tests might produce less ambiguous results.

The main study was a replication of previous research (Davidson et al., 2007) with the addition of the spatial object-locations task, therefore the same methodology was applied for administering the subtests and assessing memory retention. Although ALF is considered to manifest over very long-term delays, the intervals at which very long-term memory is tested varies widely the literature. Delays ranging from 24-hours (Bell et al., 2005) to 4 weeks (Mameniskiene et al., 2006) and even as long as 8 weeks (Blake et al., 2000) have been justified as appropriate timescales for investigating rates of forgetting. The lack of consistent findings of ALF at particular delays and the availability of only theoretical accounts of memory consolidation means that as yet, there is no clear idea of which time delays forgetting is best measured at. As well as following Davidson et al.’s protocol (2007), assessing IGE participants at 1 week was most suitable in terms of the time available for data collection, particularly when each
participant was met on 3 separate occasions. Further understanding of the timescale of ALF is needed to direct the study procedure of future research, which may be achieved by assessing memory at more than 1 very long-term delay. Although, this could introduce a confounding effect of re-learning and re-encoding of memories of the material being recalled (Butler et al., 2010).

A further limitation of the methodology concerns the use of a minimum-learning criterion to equate for initial learning. They have been applied in other ALF research (Blake et al., 2000; Butler et al., 2007) and are an effective way of ensuring that all participants have comparable amounts of information to consolidate over the delay. A criticism of the procedure is that material is repeatedly presented until the specified level of accuracy has been achieved, so participants are re-exposed to correctly recalled material across learning trials. An alternative method is to only present the material that was not recalled on the preceding trial. Bell et al. (2005) investigated ALF in temporal lobe epilepsy (TLE) patients and controls at 30 minutes and 24-hours using a selective reminding procedure. No significant differences in verbal or non-verbal memory were discovered and the rate at which material was forgotten over the 24-hours was not accelerated in the TLE patients. The absence of ALF could have been due to the alternative learning procedure. With regards to the stories subtest, because the learning criterion was set so high at 90%, participants were recalling a substantial amount of material even when they had not yet reached criterion. It is possible that participants were over-learning what they were able to recall immediately and during the first trials, which consequently may have affected the IGE and control groups’ later recall performance. A future study might incorporate a selective reminding procedure and compare the findings to those of the current study and Davidson et al. (2007). In practice, keeping track of what participants recall and then ensuring that they are presented with all the information that was not recalled, and only that information, may pose some difficulty using stories material. The selective reminding method may be more suitable with word-list material for example.

4.3 Conclusion

The ALF literature has provided new insight into the contradictory finding of normal memory functioning in people with epilepsy who complain of memory problems. Experimentally investigating very long-term memory following delays of
days or even weeks has uncovered a form of memory impairment that is not detected by standardised measures. Mostly documented in adult epilepsy populations, ALF may also be present in children with IGE; the course of forgetting in this population is dissimilar to that of healthy controls, but continued research is essential before explicit claims can be made. It is important for new and improved measures of ALF, such as the spatial object-locations task introduced here, to be improved and standardised so that they may be incorporated into neuropsychological assessment, especially in cases where memory at standard delays appears normal but memory problems are a presenting complaint. The implications of ALF for theoretical models of memory are also significant because it can inform current accounts of what is happening in memory to learned information over time. Further understanding of why ALF is most apparent in epilepsy populations and what epilepsy-related factors contribute to its manifestation must also follow.
References


Appendices

Appendix A1: NHS ethical approval

21 May 2010

Miss Katie Williams
Flat 1
10 Howden Street
Edinburgh
EH8 9HL

Dear Miss Williams

REC reference number: 10/S0709/11
Protocol number: 1

Study Title: Is accelerated forgetting a product of inefficient learning in children with idiopathic generalised epilepsy? A study incorporating a new spatial memory task

Thank you for your letter of 21 May 2010, 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/HTA R&D office prior to the start of the study (see “Conditions of the favourable opinion” below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.
Appendix A2: NHS Lothian ethical approval

Queen's Medical Research Institute  
47 Little France Crescent, Edinburgh, EH16 4TJ

DEN/MJ /approval
10/06/2010

Dr Sharon Abrahams  
The University of Edinburgh  
Department of Psychology  
7 George Square  
Edinburgh  
EH8 9JZ

Dear Dr Abrahams,

Lothian R&D Project No: 2010/C/PSY/01

Title of Research: Is accelerated forgetting a product of inefficient learning in children with idiopathic generalised epilepsy? A study incorporating a new spatial memory task

REC No: 10/50708/11  
CTA No: N/A  
Eudract: N/A  
PIS: version 1, 01/04/10  
Consent: version 1, 01/04/10  
Protocol No: version 1, 01/04/10

I am pleased to inform you that this study has been approved for NHS Lothian and you may proceed with your research, subject to the conditions below. This letter provides Site Specific approval for NHS Lothian.

Following a REC final favourable opinion, final copies of all study documentation (with revised version numbers) should be sent, with the REC letter of favourable opinion, to the R&D office.

Please note that the NHS Lothian R&D Office must be informed if there are any changes to the study such as amendments to the protocol, recruitment, funding, personnel or resource input required of NHS Lothian.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study.

Please inform this office when recruitment has closed and when the study has been completed.

I wish you every success with your study.

Yours sincerely,

[Signature]

Professor David E Newby  
R&D Director

enc  Research Governance Certificate  o (to be signed and returned)

cc  Ms Kate Williams, Dept of Psychology, University of Edinburgh, 7 George Square, 
Edinburgh EH8 9JZ  
Dr Edward Doyle, Clinical Director of Children’s Services, RHSC, Edinburgh EH9 1LF
Appendix A3: Consent from city of Edinburgh council

Katie Williams
10/1F1 Howden Street
EDINBURGH
EH8 9HL

Date 8 April 2010
Your ref
Our ref SCS/JAI
Direct dial 0131 469 3162

Dear Ms Williams

I am writing in response to your application requesting permission to undertake research in schools in The City of Edinburgh.

Your request has been considered, and I am pleased to inform you that you have been given permission in principle to undertake your research. I must stress that it is the policy of this Authority to leave the final decision about participation in research projects of this kind to Head Teachers and their staff, so that approval in principle does not oblige any particular establishment to take part.

I request that you forward a copy of your completed findings to me when they become available. In this case an electronic summary of your thesis would be preferred. Your work may be of interest to a number of staff in the Children and Families Department.

I would like to thank you for contacting the Children and Families Department about your work, and wish you every success in the completion of your project.

Yours sincerely

JULIE INNES
Administrative Officer

Mike Rosendale, Head of Schools and Community Services
Waverley Court, Business Centre 1.3, 4 East Market Street, Edinburgh EH8 8BG Tel 0131 200 2000 Fax 0131 529 6213 julie.innes@edinburgh.gov.uk
Appendix B: Toy objects used in spatial object-locations task

1) Panda soft toy
2) Yellow stretchy man
3) Dice
4) Toy car
5) Toy Watch
6) Rubber duck
7) Plastic strawberry
8) Plastic banana
9) Key
10) Rubber frog

Appendix C: Verbal instructions for spatial object-locations task

“You will be shown a board on which there are 10 toy objects. I would like you to look at each object and tell me what it is. Try to remember where each of the objects is placed because later on, I will ask you to put an identical set of objects onto a piece of paper in the same locations that you have seen them”.

Recall: “Please put these toy objects into the same places that you just saw them”.

Subsequent learning trials: “This is exactly the same board that you looked at before. Have a good look at it and try to remember where each of the toy objects is placed”.
Appendix D: The stencil used during learning trials of the spatial object-location task placed over the toy objects
Appendix E: IGE memory and educational progress questionnaire

**Your child’s memory and school progress**

1) How would you rate your child’s memory problems?  
   Please circle your choice.
   - No problems
   - A little problematic
   - Quite problematic
   - Very problematic

2) Has your child ever repeated a school year?  
   Please circle your choice.
   - Yes
   - No

3) Has your child ever received learning support?  
   Please circle your choice.
   - Yes
   - No

4) How would you rate your child’s school progress?  
   Please circle your choice.
   - No problems
   - Mildly concerned
   - Quite concerned
   - Very concerned