INVESTIGATING THE UTILITY OF THE WMS-IV^{UK} WITH NOVEL PROCEDURES AS AN ASSESSMENT TOOL FOR ACCELERATED LONG-TERM FORGETTING IN TEMPORAL LOBE EPILEPSY

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ABSTRACT

Research suggests some individuals with Temporal Lobe Epilepsy (TLE) experience an increased rate of forgetting for new information; currently defined as 'Accelerated Long-Term Forgetting' or ALF (Butler & Zeman, 2008). This novel construct goes undetected by standard neuropsychological measures and only becomes apparent after longer testing delays. However, as yet there have been no specific measures developed for the assessment of ALF. Consequentially, it is often undetected in TLE and research (relying on various novel or adapted measures) is yielding inconsistent findings.

The present study aimed to build upon the findings of a previous research project (Crowley, 2014) by adapting an existing and widely used neuropsychological measure (Wechsler Memory Scale - Fourth UK Edition [WMS-IV^{UK}]; Wechsler, 2010) in an attempt to assess its utility at detecting ALF in TLE. 25 TLE participants and 26 unaffected controls were administered selected WMS-IV^{UK} subtests with an additional one-week recall and recognition delay. Participants also completed a comprehensive neuropsychological battery of cognitive and non-cognitive measures. Data was analysed at the group and individual level, and the contribution of non-memory cognitive and non-cognitive variables was considered.

When analysed at the group level, TLE participants displayed evidence of verbal and visual ALF on selected WMS-IV^{UK} subtests, even when the mediating role of non-memory variables was considered. Individual analysis revealed a range of memory profiles in the TLE group. Some participants displayed primary difficulty in the encoding/retrieval of new information, assessed across standard delays. It was unclear whether these individuals also experienced accelerated forgetting. Other individuals displayed a memory profile consistent with current definitions of ALF and performed worse than controls at the extended delay despite performance being comparable at the standard delay. Evidence of ALF was observed for all three WMS-IV^{UK} subtests, on tasks of recall and recognition. Findings suggest the utility of the WMS-IV^{UK} at detecting ALF in TLE.

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ABBREVIATIONS USED IN THE TEXT

AEDs	Anti-Epileptic Drugs
ALF	Accelerated Long-Term Forgetting
ANOVA	Analysis of Variance
APA	American Psychological Association
EEG	Electroencephalography
IGE	Idiopathic Generalised Epilepsy
ILEA	International League Against Epilepsy
IQ	Intelligence Quotient
LM	Logical Memory
LTM	Long-Term Memory
MRI	Magnetic Resonance Imaging
NICE	National Institute of Clinical Excellence
RAVLT	Rey's Auditory Verbal Learning Task
ROCFT	Rey-Osterrieth's Complex Figure Task
STM	Short-Term Memory
TL	Temporal Lobe
TLE	Temporal Lobe Epilepsy
VPA	Verbal Paired Associates
VR	Visual Reproduction
WMS	Wechsler Memory Scale
WMS-R	Wechsler Memory Scale-Revised
WMS-III	Wechsler Memory Scale-Third Edition
WMS-IV	Wechsler Memory Scale-Fourth Edition

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In loving memory of Vera, who will never be forgotten

1. INTRODUCTION

"There seems something more speakingly incomprehensible in the powers, the failures, the inequalities of memory. ...sometimes so retentive, so serviceable, so obedient; at others, so bewildered and so weak; and at others again, so tyrannic, so beyond control."

Jane Austen, Mansfield Park

The present research is situated within the expanding field of learning and memory. It aims to assess the utility of the Wechsler Memory Scale - Fourth UK Edition (WMS-IV^{UK}; Wechsler, 2010b) with novel procedures at assessing Accelerated Long-Term Forgetting (ALF) in Temporal Lobe Epilepsy (TLE).

This section of the thesis will introduce readers to the research topic. First, an introduction to epilepsy is given, including information on definitions and classification, aetiology, epidemiology, and the psychosocial and cognitive impact. Within this sub-section the reader is also introduced to the more specific syndrome of TLE and its associated cognitive deficits. Next, learning and memory is presented, including an overview of current theory, the role of the temporal lobes, assessment methods and an introduction to ALF. A critical review of the current literature relating to ALF in TLE is provided in the third sub-section. Finally, I will outline the rationale, aims and research questions of the present study, as derived from the literature review.

1.1. Epilepsy

1.1.1. Background

1.1.1.1. Definitions and Diagnosis

Epilepsy is considered to be a neurological disorder, characterised by the presence of recurrent seizures with an unprovoked and unidentifiable cause (NICE, 2004). However, as with any medical construct, it is important to acknowledge that our current conception of this disorder is situated within the present time and place. In the past this term has been used to refer to a variety of differing concepts, and controversies surrounding the diagnosis and categorisation of the associated conditions remain (Scambler, 1989).

The most recent diagnostic system, put forward by the International League Against Epilepsy (ILAE; Fisher et al., 2014) requires (1) the presence of two or more seizures (occurring greater than 24 hours apart), (2) at least one further seizure and the probability of further seizures over the next 10 years, and (3) the diagnosis of an epilepsy syndrome, for a diagnosis of epilepsy to be made.

1.1.1.2. Seizure Classification

Epileptic seizures result from a temporary disturbance in the electrical activity of the brain (Bromfield, Cavazos, & Sirven, 2006) and vary depending on the area/s of the brain affected (Laidlaw & Laidlaw, 1980). Current classification systems (Berg et al., 2010) broadly divide seizures into the following categories; *partial* (or *focal*), *generalised* and *unknown*, with the distinction between these categories dependent on how the seizure begins. *Generalised seizures* involve abnormal neuronal discharge that simultaneously spreads to and impacts upon all areas of the brain. In comparison, *partial* or *focal seizures* describe epileptic activity that is confined to one part of the brain; and the pattern and location of abnormal neuronal discharge influences clinical presentation. Sometimes, despite commencing in one area of the brain, partial seizures will subsequently spread more globally. This is defined as a *partial seizure with secondary generalisation.*

1.1.1.3. Syndrome Classification

Different sub-types of epilepsy are referred to as epilepsy syndromes, the definition of which is dependent on a cluster of differing clinical features such as age of onset, seizure type and cause/s (Berg et al., 2010). The following dimensions are put forward by the ILAE (Berg et al., 2010) for the organisation and grouping of epilepsy syndromes:

- *Electroclinical syndromes* describe epilepsies that can be identified by a specific cluster of electroclinical characteristics, and often have a strong genetic and/or developmental component.

- *Constellations* refer to epileptic syndromes that are grouped on the basis of diagnostically meaningful lesions or conditions.

- *Structural/metabolic* epilepsies represent syndromes occurring secondary to a specific metabolic or structural pathology.

1.1.1.4. Aetiology

There is no single cause of epilepsy and aetiology varies across the clinical population (Berg et al., 2010). Causes can be conceptualised as *genetic, structural/metabolic* or *unknown* (Berg et al., 2010). *Genetic* epilepsies result from genetic defect/s and seizures represent the principle manifestation of this disorder. It is currently believed that 1-2% of all epilepsies are caused by a single gene defect (Pandolfo, 2011). However, most genetically based epilepsies are more complex and reflect the interaction between multiple predisposing genetic and non-genetic variants (Pandolfo, 2011). Conversely, s*tructural/metabolic* epilepsies are associated with a distinct metabolic or structural condition, which results in an increased risk of developing epilepsy (Berg et al., 2010). This may include brain trauma (Annegers et al., 1980), stroke (Kotila & Waltimo, 1992), infection (Lancman & Morris, 1996) and/or mitochondrial disorders (Canafoglia et al., 2001). For the majority of diagnoses cause is unknown; and a recent prevalence survey suggested over 55% of epilepsies fall into this categorisation (Benn et al., 2008).

1.1.1.5. Epidemiology

It is estimated that epilepsy currently affects 65 million people worldwide (Thurman et al., 2011), which makes it one of the most common neurological disorders (Hirtz et al., 2007). It is believed that around 600,000 people currently have epilepsy within the UK and 32,000 new cases are identified each year (Council, 2005). Figures vary globally and incidence rates are almost double among developing countries (WHO, 2009). The increased risk of head injury and brain damage faced by people living in developing countries has been put forward as an explanation for this variance. These figures illustrate the often neglected role of socio-political context and inequalities within the development of this medical disorder.

1.1.2. Impact

1.1.2.1. Psychosocial

People with epilepsy are often faced with an array of negative social and emotional consequences to their illness, including discrimination (Morrell, 2002) and inequality (Ridsdale, 2009). Research suggests that people with epilepsy are more likely to experience barriers to employment and live in poverty (Smeets, van Lierop, Vanhoutvin, Aldenkamp, & Nijhuis, 2007). People with epilepsy often report their condition has a negative impact on lifestyle, education and relationships, and this remains true even for those with good symptom control (Fisher et al., 2000). Furthermore, social stigma is still regarded as a major consequence by many (Jacoby & Austin, 2007). People with epilepsy are more likely to experience symptoms of depression and anxiety, and low self-esteem (Baker, Spector, McGrath, & Soteriou, 2005) as well as feelings of social isolation and difference (Elliott, Lach, & Smith, 2005).

1.1.2.2. Cognitive

Epilepsy is frequently associated with impairments in cognitive function (Hermann & Seidenberg, 2007). Difficulties have been observed on all key cognitive domains including attention (Zhang et al., 2009) memory (Butler & Zeman, 2008), language (Vlooswijk et al., 2010), executive functioning (Keller, Baker, Downes, & Roberts, 2009), visuospatial functioning (Williamson et al., 1992) and praxis

(Beckung & Uvebrant, 1993). Research suggests that it is often difficulties in cognitive functioning that represent the biggest concern for people with epilepsy (Fisher et al., 2000).

The nature of cognitive impairment is thought to be affected by a variety of clinical variables including age of epilepsy onset (Hermann et al., 2002), seizure type (Aldenkamp & Arends, 2004), aetiology (Jokeit & Schacher, 2004), the use of anti-epileptic drugs (AEDs) and surgery (Helmstaedter & Kurthen, 2011). The role of structural lesions within the brain (underlying epilepsy), the negative neuronal impact of seizure activity, and the mechanisms underlying seizures (even in the absence of disease or structural lesions) have all been postulated as explanations for the cognitive impairments observed in people with epilepsy (Berg, 2011). The negative side effects AEDs are also implicated (Aldenkamp, Krom, & Reijs, 2003).

It is also vital to acknowledge the impact of psychosocial variables such as low mood (Baker et al., 2005) and disrupted education (Fisher et al., 2000) upon presenting cognitive difficulties, and the importance of taking a wider systemic approach to understanding neuropsychological difficulties within this population.

1.1.3. Temporal Lobe Epilepsy

Within the field, the more specific syndrome of Temporal Lobe Epilepsy (TLE) has attracted the most attention and research. Hermann and Seidenberg (2007) attribute this to TLE being the most common of the epilepsies, as well as its tendency to develop early with an often persistent and uncontrolled course.

The syndrome of TLE is characterised by recurrent and unprovoked seizures that originate within either the medial or lateral temporal lobe (ILAE, 1989). Those affected may experience simple partial seizures, complex partial seizures, secondary generalised seizures, or a combination of the above (ILAE, 1989). It is the most common cause of partial seizures in individuals with epilepsy (Wiebe, 2000) and accounts for approximately 50% of all epilepsy diagnoses (Ko, 2014).

1.1.3.1. TLE and Cognition

Neuropsychological research within the field of TLE has yielded a generalised pattern of cognitive impairment and patients often perform worse than controls across all assessed domains of cognitive functioning (Oyegbile et al., 2004). However, it is impairments in memory that are consistently reported to represent the biggest concern (Corcoran & Thompson, 1992). The high frequency of memory difficulties reported in people with TLE has been attributed to the negative impact of seizure activity originating within the temporal lobes (Butler & Zeman, 2008); a brain structure that is currently thought to play a vital role in memory function (see Section 1.2.2.).

Interestingly, standard neuropsychological testing often fails to yield evidence of memory impairment in people with TLE and many individuals fall within the normal range when tested over standard (30-minute) delays (Fitzgerald, Mohamed, Ricci, Thayer, & Miller, 2013). However, recent research suggests that when some individuals with TLE are tested over longer delays memory difficulties can be detected and an increased rate of forgetting is seen for new information (Butler et al., 2007). This novel construct is referred to as 'Accelerated Long-Term Forgetting' (ALF) (Fitzgerald, Mohamed, et al., 2013) and provides the basis for the present research.

1.2. Learning and Memory

In an attempt to situate the present research within its broader subject matter of learning and memory, an overview of current theory, neurobiological research (specific to the temporal lobes) and assessment methods is given. ALF is also re-introduced within this context.

1.2.1. Theory

Learning and memory can be considered as two sides of the same coin: where learning refers to the acquisition of 'knowledge' and skills, memory is the term used to describe the process by which this information is stored and retrieved

over time (Matlin, 2005). Over the years, numerous theories and models have been put forward to explain the structures, processes and mechanisms of human memory (Cohen, Kiss, & LeVoi, 1993). A summary of these is provided below.

1.2.1.1. Processes of Learning and Memory

It is largely agreed that there are three main processes involved in learning and memory: encoding, storage and retrieval (McLeod, 2007) (Figure 1). *Encoding* refers to the way in which new information enters our memory, *storage* refers to the processes involved in maintaining this information over time, and *retrieval* refers to the recollection of previously stored information.

Figure 1

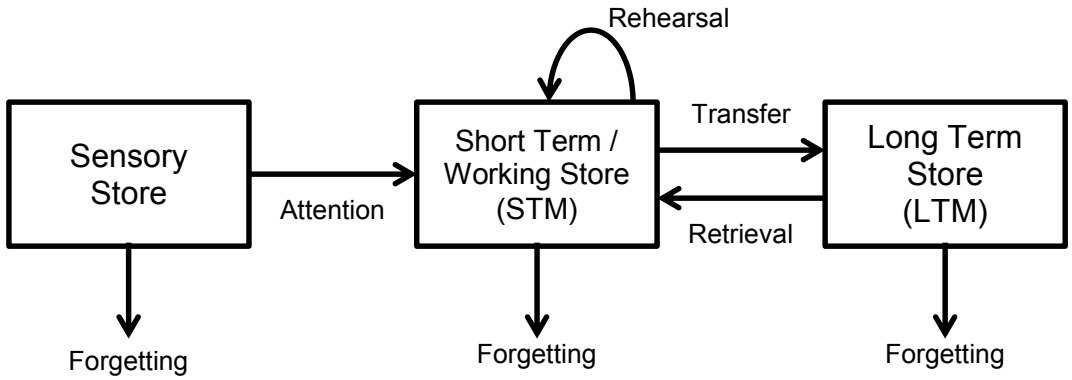
Processes of Learning and Memory: Encoding, Storage and Retrieval

1.2.1.2. Systems of Learning and Memory

The technological revolution and rise of computers in the 1960s arguably shaped current thinking around memory and the development of several models that remain dominant today (Parkin, 1993). Within these, memory is often depicted as a flow of information, governed by a number of control processes as it moves within and between three distinct systems/stores (Multistore Model of Memory; Atkinson & Shiffrin, 1968) (Figure 2). Key differences between stores are proposed in terms of function, capacity and duration.

Figure 2

The Multistore Model of Memory (adapted from Atkinson and Shriffin, 1968)

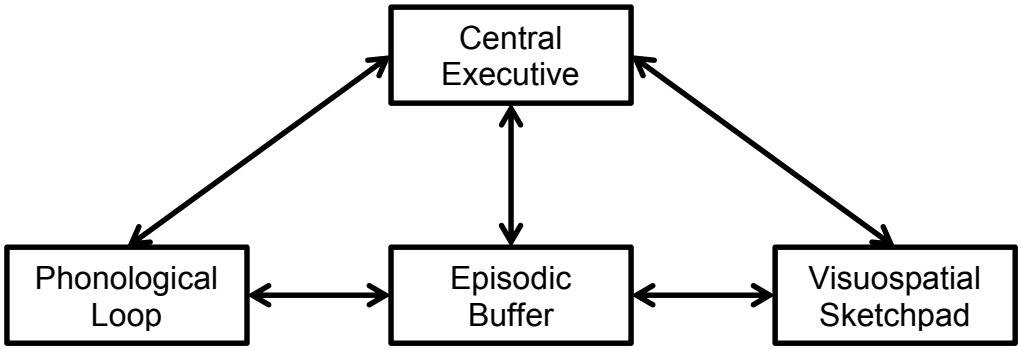


In this model, new information enters memory through an initial *sensory store*; a transitory system that holds sensory information for a matter of milliseconds. A small proportion of this information is attended to and selected, being subsequently passed onto *short-term/working memory* for further processing.

Information remains accessible within *short-term memory* (STM) for up to 30 seconds (Posner, 1966), with storage capacity limited to between five and nine 'chunks' of information (Miller, 1956). The system of *working memory* acts as an adjunct to previously more simple conceptions of STM. Dominant theories (Baddeley & Hitch, 1974) construct it as a complex and multifaceted system, with several different components that support the conscious acquisition of new information. The presence of a *phonological loop* (to hold auditory information), *visuospatial sketchpad* (for visuospatial coding), *episodic buffer* (that both holds and integrates diverse information, and communicates across the different memory systems) and overarching *central executive* (to supervise the flow of information between subservient systems) are all proposed (Baddeley, 2000) (Figure 3).

Figure 3

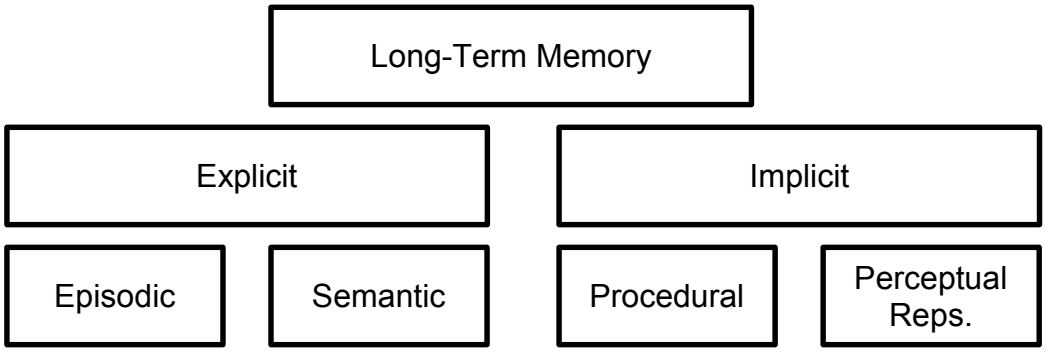
Working Memory (adapted from Baddeley, 2000)



From here, selected information is encoded into *long-term memory (LTM)*, the capacity of which is thought to be unlimited (Landauer, 1986). LTM is commonly divided between the distinctions of *explicit* (consciously recalled) and *implicit* (not consciously recalled) *memory* (Squire, 2004). Explicit memory can be further broken into *episodic* (for specific events, times and places) and *semantic* (general knowledge about the world) *memory*. In contrast, implicit memory is often divided into *procedural* (for skilled actions e.g. our ability to drive a car) and *perceptual representations* (which supports the recognition of objects, faces and/or words) *memory* (Figure 4).

Figure 4

Long-Term Memory Systems



1.2.1.3. Consolidation Theory

Consolidation refers to the gradual reorganisation process by which new information is permanently stored into LTM (Squire & Alvarez, 1995). It is suggested that newly encoded information is initially stored within the hippocampus for periods of up to one week (Frankland & Bontempi, 2005). From here, information is gradually re-organised and transferred into the neo-cortex for permanent storage where it becomes independent of the hippocampus (Dudai, 2004). Prior to this, memories remain vulnerable to retroactive interference (Lechner, Squire, & Byrne, 1999). This process of memory consolidation is put forward to account for the fragility of newer memories, as has been observed in retrograde amnesia (Burnham, 1903).

1.2.1.4. Forgetting

Forgetting refers to the inability to recall/recognise previously perceived information (Parkin, 1993). Forgetting is thought to occur for a variety of reasons including the failure to correctly encode new information (Richardson, 1993), the gradual decay or loss of previously stored information due to the passage of time (Ebbinghaus, 1885) and/or the failure to appropriately retrieve previously stored information, which could be due to interference from newly acquired information (Tomlinson, Huber, Rieth, & Davelaar, 2009). Ebbinghaus' (1885) theory suggests that forgetting from LTM follows a logarithmic curve and occurs rapidly in the initial period after encoding, before levelling off as its rate progressively decreases. This is in line with single-consolidation-process models of LTM (Squire & Alvarez, 1995), which also intimate the instability of newer memories (before consolidation into more permanent brain structures).

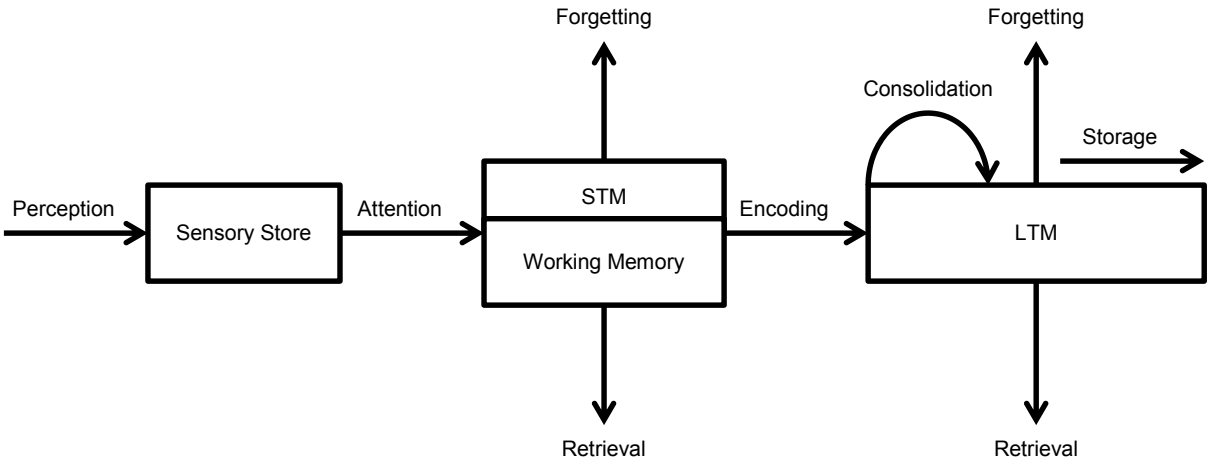
1.2.1.5. Summary

To summarise, contemporary constructions of memory rely upon three key processes of encoding, storage and retrieval. Furthermore, memory is suggested to comprise several distinct sub-systems through which new information is perceived, attended to, operated upon, stored and retrieved. These include sensory, short-term/working and LTM stores. The complex and interrelated nature of memory means that there are many ways for this system to become

disrupted: effective memory processing thus requires all levels to remain intact (Figure 5).

Figure 5

Diagrammatic Summary of Memory Systems and Processes



It is worth making explicit that the concept of human memory (as well as all of its theorised systems and processes) is socially constructed. Therefore, although our current understanding of memory as a human entity is often reified through discourse, it is important to acknowledge memory as a construct that relies on the metaphorical flow of information through several distinct systems/stores. This construct is not aligned with fact but shaped and dependent upon the context in which it arose.

1.2.2. The Temporal Lobes and Memory

The temporal lobes (TL) are currently put forward as the most important brain region underlying the formation and storage of long-term memory (Squire & Zola-Morgan, 1991). Verbal memory is classically associated with the left TL, whereas visual memory appears to be situated in the right (Milner, 1971). Within the TLs, several key structures have been identified. These include the medial TL and diencephalon, which appear to play an important role in the processing, storage

and retrieval of both episodic and semantic memory (Squire, 2004). Furthermore, the hippocampus, which lies within the medial TL (Kolb & Whishaw, 2009), is believed to be vital to the re-organisation and consolidation of long-term episodic memories (Squire & Zola-Morgan, 1991).

The high frequency of memory difficulties that present in people with TLE is often attributed to the negative neuronal impact of seizure activity, which originates in the TLs (Butler & Zeman, 2008). TLE seizure characteristics (e.g. frequency, location of onset, severity) are shown to mediate dysfunction within this brain region, and in turn contribute to an associated pattern of memory impairment (Oyegbile et al., 2004).

1.2.3. Methods of Assessment

1.2.3.1. Assessing Short-Term and Working Memory

The acquisition of information into STM can be assessed using a variety of measures (Lezak, Howieson, Bigler, & Tranel, 2012). Typically, digit and spatial spans are used to assess verbal and visual domains respectively. In terms of working memory, digit reversal or sequencing can be used to assess verbal operations whereas tasks such as spatial addition (Wechsler, 2009) can be utilised for the visual domain.

1.2.3.2. Assessing LTM

Measures of LTM tend to follow a standard design. First, participants undergo a learning phase during which new information is presented. Information may be presented once (Randolph, 1998), for a fixed number of trials (Wechsler, 2009) or until a learning criterion has been met (Schmidt, 1996): comparison between these methods can be used to assess the effect of repetition on learning/memory. Examinee's ability to free recall and/or recognise the information is then assessed and will support the examiner to differentiate between difficulties in retrieval as opposed to retention (Lezak et al., 2012). Assessment of initially presented information takes place both immediately (as a measure of encoding) and then again after a standard 30-minute delay (as a measure of longer term retention) (Randolph, 1998; Schmidt, 1996; Wechsler, 2009). Additional

measures are administered between task intervals to prevent rehearsal. Verbal LTM is usually assessed using tasks of story recall/recognition (which measure semantic-episodic ability) and word pair/list learning (which provide a measure of material-specific information). In comparison, figure drawing and spatial location learning can be utilised to assess visual ability (Lezak et al., 2012).

1.2.3.3. Wechsler Memory Scale (WMS)

This battery comprises a comprehensive assessment of adult memory. The most recent edition, Wechsler Memory Scale - Fourth Edition (WMS-IV; Wechsler, 2009) is currently the most widely used memory test (Drozdick, Holdnack, & Hilsabeck, 2011). It includes measures of both verbal and visual working, immediate and delayed memory.

Within the field of TLE, the WMS has been the most commonly utilised measure (Jones-Gotman, 1993). However, as yet little data has been published on the validity of its newest edition with this population (Loring & Bauer, 2010). Furthermore, research assessing the validity of its predecessor, Wechsler Memory Scale - Third Edition (WMS-III; Wechsler, 1997) within the field of epilepsy is both sparse and results are not consistent. The majority of papers appear to suggest the WMS-III has limited utility in differentiating laterality (the brain hemisphere of seizure onset) in people with epilepsy (Baker, Austin, & Downes, 2003; Wilde et al., 2003; Wilde et al., 2001) and Wechsler (2009) suggests that the measure is likely to be more sensitive to left than right TLE. On the other hand, Wilde et al. (2003) have supported the utility of the WMS-III at differentiating between working and LTM in people with epilepsy and Doss, Chelune and Naugle (2004) suggest it to be effective at detecting hemispheric lateralisation in epilepsy patients following temporal lobectomy. Additional research is clearly needed to assess the validity of the WMS-IV at detecting the variety of memory deficits presenting in TLE.

1.2.3.4. Considerations

The standard neuropsychological assessment process appears to substantially align itself with current theories of memory consolidation (Squire & Alvarez, 1995) in the assumption that consolidation is a unitary process and therefore the

efficacy of LTM should be amenable to assessment after relatively short (currently 30-minutes as standard) delays. On the other hand, this current assessment paradigm could be seen to stand in some conflict with present understandings of memory consolidation, which suggest the re-organisation and transfer of new memories into longer-term and more permanent stores can take up to one week (Squire & Alvarez, 1995). Based on this potential tension, it is arguable that additional measures (following one-week delay) should be included in a comprehensive assessment of LTM if the assessor wishes to gain an accurate and ecologically valid measure of memory function.

It is also noted that alongside memory, a comprehensive assessment should consider the functioning of all other cognitive domains (e.g. attention, language, visuospatial and executive function) as impairment in any of these areas will have an effect on memory processing (Lezak et al., 2012). Similarly, the vast array of non-cognitive factors that can impact upon test performance must also be taken into account when interpreting test scores (Lezak et al., 2012). Furthermore, assessors must acknowledge that any attempted measurement of memory will be indirect and only provide data on the hypothesised output of this construct within context.

1.2.4. Accelerated Long-Term Forgetting

ALF refers to a novel memory condition, which results in the exacerbated forgetting of new information (Butler & Zeman, 2008). This increased rate of forgetting appears to develop after the standard neuropsychological testing delay despite apparently normal encoding, storage and 30-minute delayed retrieval of novel information (Fitzgerald, Mohamed, et al., 2013).

Ahern et al. (1994) first documented the phenomenon in their description of 45-year-old JT who presented with TL seizures three years prior. When assessed using standard neuropsychological measures, JT's new learning appeared intact. However, when questioned several days later JT showed an accelerated rate of forgetting for this information, undetected by standard assessment tools.

To date, the majority of research into ALF has described this phenomenon in people with TLE (Fitzgerald, Mohamed, et al., 2013). However, its presence has also been documented in other epilepsy syndromes (Davidson, Dorris, O'Regan, & Zuberi, 2007; Kapur et al., 1996) as well as people with head injury and brain trauma who did not have an epilepsy diagnosis (De Renzi & Lucchelli, 1993; Smith et al., 2010). Due to the scope of the present research, the review will be limited to ALF in TLE.

ALF has been put forward to explain the high prevalence of subjective memory difficulties reported in people with TLE, which are often not picked up by standard neuropsychological measures (Fitzgerald, Mohamed, et al., 2013). Its presence is suggested to reflect an impairment of memory consolidation (Gallassi et al., 2011) and challenges the single-consolidation-process models of LTM (Squire & Alvarez, 1995) that standard neuropsychological measures reflect. Instead, the construct of ALF appears to support the presence of a more complex and multiple-stage LTM consolidation process (Butler & Zeman, 2008).

1.3. Literature Review: ALF in TLE

An exhaustive review of the literature relating to ALF in TLE was conducted across PsychInfo, Pubmed, CINAHL and Medline within an unrestricted timeframe. Searches were conducted between November 2013 and April 2015. Search terms "epilepsy", "temporal lobe epilepsy", "accelerated long-term forgetting" and "long-term amnesia" (LTA; Kapur et al., 1996) were inputted in various combinations. All case and group studies relating to ALF in people with TLE were included. Papers relating to ALF occurring outside TLE were excluded. The reference lists of all (case, group and review) papers relating to ALF in TLE were also searched for unidentified literature.

1.3.1. Case Studies

10 case studies relating to ALF in TLE were identified. A critical review of this literature is provided below. Findings are discussed in terms of the

neuropsychological impact of ALF in TLE. Studies that investigated verbal ALF are reviewed first, followed by a discussion of research that investigated both verbal and visual ALF simultaneously. See Appendix 1 for an overview of methods and findings.

1.3.1.1. Case Studies of Verbal ALF

Several case studies focused on ALF solely within the verbal domain. This includes research by Jansari et al. (2010) who used novel stories to assess verbal recall and recognition in participant RY. Results suggested evidence of ALF in RY's story recall at 24 hours and recognition at one week. This was despite apparently normal performance following a standard 30-minute delay. Differences in RY's recall and recognition memory performance suggest recognition may be more resistant to ALF. However, interpretation surrounding the exact onset of ALF for each of these abilities is limited by the infrequency of utilised testing delays.

The introduction of additional delayed testing points enabled McGibbon and Jansari (2013) to detect ALF in RY at just 55 minutes and suggests the point of onset may not be too far from the delays currently utilised in clinical practice. Within both studies (Jansari et al., 2010; McGibbon & Jansari, 2013), researchers also demonstrated the elimination of ALF through repeatedly reviewing the to-be-learnt information, intimating the potential benefit of this as a behavioural strategy. It is possible that the inherent nature of repeatedly reviewing new information within everyday life may result in a lack of awareness of this impairment, and contribute to the currently poor detection rates and uncertainty surrounding prevalence. However, as both studies assessed the same TLE participant, questions are raised around the generalisability of findings. Additionally, the failure of these studies to assess RY's performance across other cognitive domains known to mediate verbal memory performance (e.g. attention and verbal fluency; Lezak et al., 2012) further limits understanding of this presentation.

A study by O'Connor et al. (1997) also utilised more regular testing delays than Jansari et al. (2010) but was unable to detect verbal ALF until eight hours.

Findings raise the possibility that the point of onset for ALF may differ across those affected. However, the use of just one un-matched control for comparison in the O'Connor et al. (1997) study raises questions about the validity of findings. Furthermore, variation between studies in terms of assessment tool and design challenges any interpretations made across findings.

1.3.1.2. Case Studies of Verbal and Visual ALF

Interestingly, there appear to be no case studies focusing solely on ALF in the visual domain. However, several have investigated the presence of both verbal and visual ALF in a single client, and found varying results.

Mayes et al. (2003) reported the simultaneous occurrence of both verbal and visual ALF in JL whose recall and recognition was assessed following three weeks delay. However, JL also performed significantly worse than controls on visual measures at the standard 30-minute delay. Results suggest that this participant may experience visual memory deficits aside from ALF and question the researchers' attribution of extended visual task performance to ALF.

Manning et al. (2006) also reported verbal and visual ALF in a single TLE participant, assessed with novel story recall and face recognition tasks. Interestingly, visual ALF was not detected until one week, compared to verbal ALF, which was reported from 30 hours. This may illustrate a distinction between ALF that occurs in the visual and verbal domain. Alternatively, this difference may reflect variation in task demand, with researchers utilising an arguably easier recognition task to assess visual memory. Furthermore, facial recognition is regarded as a distinct ability (Bruce & Young, 1986); the utility of this task as a measure of visual ALF is therefore questionable.

Kemp, Illman, Moulin and Baddeley (2012) recorded an interesting pattern of results. ALF was detected for verbal recall at 11 days, however by 28 days their participant SK's performance had returned to the level of controls. In comparison, SK's performance on verbal recognition was markedly worse than controls at both 11 and 28 days, and challenges the previous suggestion of recognition memory as more resistant to ALF. In terms of visual recall, SK's

performance was again significantly worse than controls at both extended testing delays. SK's variable pattern of forgetting could suggest ALF reflects a fluctuating deficit in the retrieval of previously encoded memory, opposed to the exacerbated decay of new information. Alternatively, it may be that accelerated forgetting is not linear but peaks before levelling off after an extended period of time. This idea is supported by Cronel-Ohayon et al. (2006) who demonstrated evidence of verbal and visual ALF in participant JE that reduced in severity over the period of one month. However, validity of these findings is limited by the use of just one control for comparison. Furthermore, returning to Kemp et al.'s (2012) paper, interpretation is once again arguably flawed by their TLE participant's recorded difficulties in the learning phase of both verbal and visual tasks, which question whether results are more representative of an initial encoding deficit.

Gallassi et al. (2011) investigated verbal and visual recall using Babcock's story, Rey's Auditory Verbal Learning Task (RAVLT) and Rey-Osterrieth's Complex Figure Test (ROCFT). Evidence of ALF was demonstrated on the word list and figure but not story task. Findings suggest a distinction between ALF for visual, verbal semantic-episodic and verbal material-specific information. However, impairments were also found in verbal function; failure to consider the potentially mediating effect of difficulty in this domain hugely limits the validity of findings. Contrasting Gallassi et al.'s (2011) findings, Lucchelli and Spinnler (1998) demonstrate evidence of ALF on Babcock's story but not ROCFT, and further support the idea of a distinction between verbal and visual ALF. However, once again findings are limited by control group size (N=2).

Finally, Kapur et al. (1997) found evidence of ALF for verbal recall and recognition as well as visual recall at six weeks delay, whilst visual recognition remained intact. Once again, distinction between the effects of ALF in terms of verbal / visual divide as well as recall / recognition ability is suggested. However, this study's failure to provide up to date information on their TLE participant's performance across the other cognitive domains questions the potential role of impairment on mediating cognitive variables.

1.3.1.3. Summary

The case study literature intimates the presence of both verbal and visual ALF in TLE. Findings are varied; and differences are reported in terms of onset (Jansari et al., 2010; McGibbon & Jansari, 2013; O'Connor et al., 1997), distinctions between ALF for visual / verbal information (Gallassi et al., 2011; Kemp et al., 2012; Mayes et al., 2003) and recall / recognition memory (Kapur et al., 1997; Manning et al., 2006; McGibbon & Jansari, 2013).

Findings are all limited by the single-participant nature of case study research. Further to this, many of the studies also utilise single-participant control groups (Cronel-Ohayon et al., 2006; Lucchelli & Spinnler, 1998; O'Connor et al., 1997), which strongly questions the representativeness of comparisons made. Interpretation across these studies is also limited by the vast array of tools and research designs utilised. Furthermore, few studies assessed for non-memory cognitive impairments, which are both highly prevalent in TLE (Oyegbile et al., 2004) and strongly correlated with memory difficulty (Lezak et al., 2012). Although these papers provide a basis for interpretation, further analysis of the more recent group study literature is clearly necessary before any less tentative conclusions can be drawn.

1.3.2. Group Studies

24 group studies relating to ALF in TLE were identified. Findings are discussed in terms of (a) the neuropsychological impact of ALF, (b) the neural basis and (c) mediating variables. See Appendix 2 for an overview of methods and findings.

1.3.2.1. Neuropsychological Impact

As with the case study literature, group research has used a variety of measures to assess ALF in TLE (Butler et al., 2009; Djordjevic et al., 2011; Narayanan et al., 2012). The phenomenon is demonstrated on tasks of recall (Butler et al., 2007; Wilkinson et al., 2012) and recognition (Bengner et al., 2006; Manes, Graham, Zeman, Calcagno, & Hodges, 2005) within both verbal (Blake, Wroe, Breen, & McCarthy, 2000; Martin et al., 1991) and visual (Giovagnoli, Casazza, &

Avanzini, 1995; Mameniskiene, Jatuzis, Kaubrys, & Budrys, 2006) memory modalities.

1.3.2.1.1. Group Studies of Verbal ALF

Several group studies have focused on ALF within the verbal memory modality. This is true of Martin et al. (1991) who demonstrated ALF in their group of 21 TLE participants using the selective reminding test. Although no differences were detected at the standard 30-minute delay, TLE participants performed significantly worse than controls on tasks of recall at the 24-hour delay. In contrast, recognition was not impaired. It is possible that additional impairment for this ability may have been detected if the researchers had utilised longer testing delays. Hoefeijzers, Dewar, Della Sala, Zeman and Butler's (2013) study supports this idea, and demonstrates TLE group ALF on RAVLT for verbal recall at one week and verbal recognition at three weeks. In line with case-study research (Kapur et al., 1997; McGibbon & Jansari, 2013), findings support a distinction between ALF for recall and recognition memory. However, both papers can be criticised for failing to provide single participant analysis, which limits understanding about the proportion of TLE participants affected by ALF within their samples, whether both affected and unaffected participants were included, and if so how this may have diluted the differences observed between groups.

Studies by Blake et al. (2000), Butler, Kapur, Zeman, Weller and Connelly (2012), Djordjevic et al. (2011), and Deak, Stickgold, Pietras, Nelson and Bubrick (2011) also all focused solely on ALF within the verbal memory domain and used a variety of different measures to successfully demonstrate its presence when assessed across a larger group; findings are discussed in more detail in subsequent sections of the review.

1.3.2.1.2. Group Studies of Visual ALF

To my knowledge, only one of the group studies that focused solely on visual ALF was successful in demonstrating its presence. Bengner et al. (2006) compared 56 TLE participants to 12 controls using novel face recognition. Evidence of ALF was found for right TLE participants with normal MRI scans at

24 hours. In comparison, right TLE participants with abnormal MRI scans were immediately impaired in performance and displayed difficulties in learning opposed to accelerated forgetting. Results confirm a distinction between systems underlying learning and memory and suggest the role of right TLE in accelerated forgetting of faces. However, the distinct nature of face recognition (Bruce & Young, 1986) restricts interpretation to this specific facet of visual memory. Furthermore, results are limited by the study's failure to assess for non-memory cognitive impairments known to affect visual memory (e.g. attention and visuospatial function; Lezak et al., 2012), or investigate the potentially mediating role of the differences observed between their groups in IQ performance and mood.

Discussion about the role of TLE hemispheric lateralisation in ALF as well as an overview of visual domain specific research that has failed to demonstrate ALF in TLE will be revisited later in the review.

1.3.2.1.3. Group Studies of Verbal and Visual ALF

The majority of group research has investigated the presence of verbal and visual ALF simultaneously. A selection of papers that successfully demonstrate ALF is discussed below. Many find differences between verbal and visual memory performance and suggest a distinction between ALF as it presents across these domains. Research assessing visual and verbal ALF simultaneously, and failing to detect this construct, is discussed later.

Butler et al. (2007) reported verbal and visual ALF in their TLE group. In terms of visual material, no between-group differences were found at 30-minute recall when assessed using Graham-Kendall's Memory for Designs task. However, impairment (ALF) was apparent at one week. Similarly, impairment was evident at one week on the verbal task (RAVLT), which was also interpreted as ALF. However, this could be questioned as TLE participants also performed worse on RAVLT at 30 minutes. It therefore appears more likely TLE participants' RAVLT performance at one-week was reflective of an impairment in initial verbal memory consolidation opposed to ALF.

Manes, Graham, Zeman, Calcagno and Hodges (2005) also reported evidence of visual and verbal ALF when assessed across a group of seven TLE participants. No differences were found between groups at the standard 30-minute delay, however when participants were re-assessed at six weeks the TLE group displayed ALF for both verbal recall and recognition. Similarly, by six weeks TLE participants had no recall ability for the visual design task and all produced a score of zero. As a result the authors chose to eliminate this data and do not put it forward as evidence of visual ALF. However, contradictory to this decision, I would argue that these findings clearly demonstrate evidence of ALF in the visual domain. Interestingly, no differences were found between groups on the visual recognition task, which once again suggests differences between ALF for verbal and visual memory.

Muhlert et al.'s (2011) study assessed both verbal and visual ALF in a group of 14 TLE patients, 14 ideographic generalised epilepsy (IGE) patients and 15 healthy controls. ALF was demonstrated in the TLE group at three weeks on tasks of visual recall and story recognition. Findings intimate specificity of ALF to TLE opposed to IGE. Interestingly, TLE participants' performance on story recall appeared well preserved. This contradicts previous research that has found recall to be more strongly affected than recognition (Jansari et al., 2010; Kapur et al., 1997; Manning et al., 2006) and research that suggests visual memory is less susceptible to ALF (Butler et al., 2007; Kemp et al., 2012). Once again findings are limited by the study's failure to investigate potentially mediating cognitive variables or provide single participant analysis.

In comparison, Helmstaedter, Hauff and Elger's (1998) paper put forward a similar pattern of ALF for both visual and verbal stimulus. Their group of 55 TLE participants performed significantly worse than controls at one week across all tasks. However, TLE participants also performed worse during the learning phases, which again questions whether findings demonstrate ALF or an initial encoding deficit.

The studies above provide evidence of ALF occurring in both verbal and visual memory domains when assessed in a larger group setting and with a variety of

measures. Many of the studies appear to suggest that ALF affects verbal and visual memory differently, however findings are in no way unanimous. Reported differences between control and TLE participants (previously unidentified as experiencing ALF) appear to portray a certain commonality to this experience within TLE. However, single participant data is not reported, making it difficult to extrapolate how prevalent ALF was within the TLE group; the likely inclusion of individuals both affected and unaffected by ALF will have diluted differences observed between groups. Furthermore, studies are limited by their failure to investigate the potentially mediating role of impairment across other cognitive variables known to affect memory function, as would be standard practice in neuropsychological assessment before any domain-specific interpretation (Lezak et al., 2012).

1.3.2.1.4. Group Studies without ALF

The existing group literature appears to portray a certain universality to the experience of ALF in TLE. This is exacerbated by failure to present single-participant data, making it hard to extrapolate what proportion of participants were affected. However, there are several papers that present a different picture in their inability to detect the presence of this novel construct.

Bell, Fine, Dow, Seidenberg and Hermann (2005) failed to detect differences between their substantial group of 42 TLE and 49 control participants when assessed using the selective reminding task. Although differences were found between TLE and control groups during the learning and both recall phases, no differences were found in terms of forgetting rate. This was also true when data was analysed at the individual level. Unlike much of the previous research within this review, findings portray ALF as a relatively unusual experience in TLE. It is possible that the selective reminding task is not appropriately sensitive to detect ALF or that an extended testing delay of just 24 hours is too short, with comparable research methods by Lucchelli and Spinnler (1998) and Deak et al. (2011) unable to detect ALF before one week. However, research by Martin et al. (1991), who successfully identified ALF using the selective reminding task as well as papers by Bengner et al. (2006), Djordjevic et al. (2011) and Muhlert et al. (2010), who all detected ALF at 24 hours, suggests otherwise.

Similarly, Bell's (2006) study failed to detect ALF in a different sample of 25 TLE participants using a more widely recognised neuropsychological measure (WMS-III) and a longer (two-week) delay. Once again, the TLE group performed worse than controls in the learning and both recall trials, however no differences were found in information retention between trials. Findings are strengthened by additional single-participant analysis, which also failed to detect between-group differences.

Finally, Giovagnoli, Casazza and Avanzini's (1995) paper also failed to find evidence of ALF. Although differences were found between TLE and control participants during the learning phase (with control participants' able to learn significantly more novel information), no differences were seen between groups in percentage recall over several extended delays. As with Bengner et al.'s (2006) paper, this study demonstrates a distinction between systems of learning and memory, and suggests learning impairments in TLE may not result in difficulties retrieving stored information. It is possible that the additional inclusion of single-participant analysis could have provided evidence of ALF in a minority of Giovagnoli et al.'s (1995) TLE participants', whose differential memory profiles may have been diluted by the larger group analysis. However, taken together these studies suggest ALF may not be as commonplace in TLE as has been portrayed by much of the existing literature.

1.3.2.1.5. ALF Outside of the Laboratory

The majority of research has investigated ALF in TLE using standard neuropsychological measures within a laboratory-based environment. As a result little is known about the impact of ALF in everyday life settings and to my knowledge only two papers have addressed this issue.

Muhlert, Milton, Butler, Kapur and Zeman (2010) assessed participants' memory for photographs taken while visiting a local attraction, for a standardised word list and a procedural memory task. Results demonstrate evidence of ALF for the photographs in the TLE group at 24 hours and suggest this novel memory impairment does affect autobiographical memory for events outside of a laboratory setting. However, the use of photographs as a measure of

autobiographical memory is questionable; real life events rely on a combination of verbal, visual, episodic and semantic memory, which photograph recognition is unlikely to reflect. Interestingly, ALF was not detected on the procedural memory task, which may suggest ALF is specific to declarative memory. This is an area in need of further investigation.

Tramoni et al. (2011) assessed the memory of five TLE participants across a series of contextually bound (and thus more generalisable to real life) tasks. No differences were found between TLE participants and controls following a short delay, however after six weeks TLE participants' performance was significantly worse. The inclusion of a comprehensive neuropsychological test battery, across which no between-group differences were found, adds additional credibility to these findings.

In line with the memory difficulties reported by many people with TLE (Piazzini, Canevini, Maggiori, & Canger, 2001), the above studies demonstrate the negative impact of ALF on people's memories from everyday life and further enforce the need to develop standardised assessment tools within this area.

1.3.2.2. The Neural Basis of ALF

Several papers have used imaging to investigate the neural basis of ALF in TLE and present both varying and inconclusive data. Butler et al. (2009) found no relationship between TL atrophy and ALF when assessed across a group of 22 TLE participants whose overall performance suggested evidence of ALF on both verbal and visual measures. Findings are somewhat limited by the researchers' decision to combine participants' scores across all memory tasks to provide one generic measure of ALF, consequentially losing potentially meaningful information about the relationship between different sub-types of ALF (e.g. verbal versus visual) and TL atrophy. However, taken at face value findings appear to suggest that the basis of this construct may exist outside of the TLs.

Contradictory to this idea, Butler et al.'s (2012) whole-brain MRI analysis failed to identify any gross anatomical correlates of ALF. However, it is worth acknowledging that their TLE participants also performed significantly worse than

controls following a standard 30-minute delay, questioning whether the differences detected (at the extended delay) were a result of ALF or a more generic memory deficit. Therefore, the failure of this paper to find any anatomical correlates may have been a consequence of analysing an unaffected sample.

Although Butler et al. (2013) demonstrated neurological hippocampal differences in their TLE group (who were suggested to display evidence of ALF) differences were related to anterograde memory performance opposed to ALF. As this study investigated the same group of TLE participants as Butler (2012), questions surrounding the validity of ALF interpretations remain.

In contrast, Wilkinson et al. (2012) put forward a relationship between structural hippocampal abnormality and ALF that was detected at one hour in a sub-group of TLE participants. However, this research failed to assess memory after a standard 30-minute delay. It is therefore impossible to conclude whether findings reflect more generic LTM difficulties or ALF. Considering this, it is possible the differences found in hippocampal pathology reflected initial impairments in storage and/or retrieval opposed to ALF. Furthermore, no relationship was found between hippocampal pathology and the sub-group of TLE participants who displayed ALF after six weeks, which appears to contradict the author's suggestions of a role for this structure in ALF.

Narayanan et al. (2012) has also postulated the role of the hippocampus in ALF. However, their TLE participants showed memory deficits at 30 minutes as well as following extended delays. Whether findings demonstrate a relationship between hippocampal abnormality and ALF or a more generic memory deficit is uncertain.

Finally, Lah et al. (2014) found a relationship between hippocampal lesions and onset of ALF, with TLE participants displaying lesions to the hippocampus developing ALF from 1 day. In comparison, TLE participants with intact hippocampi did not display ALF until 7 days. Results suggest a role for this brain structure in mediating the onset of ALF, but do not support a hypothesis for the neural basis of this construct originating within the hippocampus. Findings are

limited by the study's failure to assess between-group difference on mediating cognitive and non-cognitive variables.

Taken together, findings raise several questions. Firstly, despite the failure of the above studies to identify a neural basis, it remains possible ALF results from subtle structural or functional disturbance/s undetectable by neural imaging (Butler et al., 2012). Alternatively, the basis of ALF may not be neural, or the evidence provided above may not be reflective of ALF. Findings could also be put forward as questioning the validity of ALF as a reliable construct.

1.3.2.3. Mediating Variables

The group literature has put forward a variety of mediating variables in the development and experience of ALF in TLE. These include seizure lateralisation, epileptic activity and sleep. Although not yet investigated specifically by the existing evidence-base, the role of psychiatric and cognitive variables is also considered.

1.3.2.3.1. TLE Lateralisation and ALF

Earlier, the potential relationship between right TLE and visual ALF was put forward (Bengner et al., 2006). The role of TLE hemispheric lateralisation in the specialisation of ALF to either verbal or visual memory is further supported by the following studies.

Djordjevik et al. (2011) found a relationship between left TLE and ALF on a verbal task. In comparison, right TLE participants' performance matched that of controls, which may suggest left TLE is specific to verbal ALF. However, as the research utilised only one delayed testing point (with recall assessed at either 30 minutes or 24 hours), which prevented any comparisons being made between a standard and extended delay, it is difficult to assess whether these reported impairments were reflective of ALF or a more generic memory deficit. The fact that left TLE participants required more trials in the learning phase appears to support the later interpretation.

Blake et al.'s (2000) findings also support the relationship between left TLE and verbal ALF. Their study found no differences between controls and TLE participants when assessed on a task of verbal memory after a standard 30-minute delay. However, after eight weeks evidence of ALF was detected in left but not right TLE participants. Findings could have been enhanced with the use of additional visual memory tasks to assess whether the opposite effect occurred in the right TLE group.

Research investigating both verbal and visual ALF simultaneously also appears to intimate the mediating role of TLE lateralisation. Narayanan et al. (2012) found left TLE participants showed significantly faster forgetting rates for verbal information following extended delay. This was compared to right TLE participants who showed a trend (approaching significance) towards visual ALF. However, it is noted that impairments in learning as well as recall and recognition following the standard 30-minute delay were also found in both TLE groups. This again questions whether findings demonstrate evidence of ALF or a more generic memory deficit.

Taken together, results appear to support a relationship between TLE hemispheric lateralisation and the sub-domain of memory affected by ALF; with visual ALF apparently related to right TLE and verbal ALF linked with left.

1.3.2.3.2. Epileptic Activity

Fitzgerald, Thayer, Mohamed and Miller's (2013) study suggests the potential role of subclinical discharge (abnormal electrical brain activity occurring in the absence of overt clinical signs or symptoms) in ALF. Although initial analysis found no differences in forgetting between TLE and control participants over a series of extended delay, when separated in terms of epileptic activity differences were found. Participants who experienced focal discharges displayed ALF for verbal information at 24 hours. In comparison, participants who experienced generalised discharges displayed ALF for visual information at four days. Findings suggest subclinical discharge may play a role in the sub-domain of memory affected by ALF. However, results are somewhat limited by the use of

novel and previously unstandardised tools to assess memory, which raises questions of construct validity and generalisability of findings.

Seizure frequency has also been related to ALF in TLE, and Mameniskiene et al. (2006) found a positive relationship between seizure frequency and forgetting rate in their TLE group at four weeks. This was true even for TLE participants whose performance did not differ to controls at the standard 30-minute delay. Additionally, Evans et al. (2014) found surgery (that controlled seizure activity) led to improvements in both verbal and visual ALF, which further supports for the relationship between epileptic activity and this novel construct. However, additional individual-level analysis suggested only one TLE participant displayed a profile consistent with current definitions of ALF, which questions the validity of Evans et al.'s (2014) group-level analysis/interpretation.

Taken together, results of the studies above suggest the role of uncontrolled seizure activity in ALF in TLE and highlight the necessity of further research into epilepsy treatment and management to reduce the negative cognitive impact of recurrent seizures. However, not all research has produced consistent findings, and research by Mulhert et al. (2011) failed to find any association between seizure activity and ALF in their group of TLE participants. Thus illustrating the complexity of any assumed relationship between epileptic activity and ALF, the likelihood of further interacting variables within this relationship, and the necessity of continued research within the area.

1.3.2.3.3. Sleep

Deak et al. (2011) assessed the relationship between sleep and ALF in TLE. Findings suggest evidence of verbal ALF after an extended (12 hour) delay. However, this was only for TLE participants tested after 12 hours of daytime wake, compared to those who were assessed after a night's sleep. This study implicates sleep as a mediating factor within the experience of ALF and suggests its potential role in the consolidation of memory. Replication of these findings in a larger sample (with the present study assessing only six TLE participants) with administration of both visual and verbal measures is necessary to strengthen the validity of findings.

1.3.2.3.4. Psychiatric Variables

Research suggests the role of psychiatric variables in mediating cognitive function; and symptoms of anxiety and depression have been related with impairments in learning and memory (Dalgleish & Watts, 1990). As already discussed, a higher prevalence of psychiatric diagnosis is found in people with epilepsy (Baker et al., 2005). Furthermore, current research investigating ALF has consistently found people with TLE score higher on measures of anxiety and depression (Butler et al., 2009; Butler et al., 2007; Mameniskiene et al., 2006).

Despite the above, as yet there has been no evidence to suggest the mediating role of psychiatric diagnosis on ALF in TLE (Butler et al., 2009; Butler et al., 2007; Mameniskiene et al., 2006). However, the well-documented relationship between psychiatric variables and memory performance demands future research continue to consider the influence of between-group difference in this area of function.

1.3.2.3.5. Cognitive Variables

Non-memory cognitive variables have also been shown to mediate memory performance. For example, impairments in attention (Robinson, 1995), executive (Duff, Schoenberg, Scott, & Adams, 2005), general verbal and visuospatial function (Park et al., 2002) have all been related to difficulties in learning and memory.

Research suggests that individuals with TLE often score lower than typically developed controls on all areas of cognitive function (Hermann & Seidenberg, 2007). However, the majority of research investigating TLE has only assessed for differences on measures of intelligence (IQ) (Blake et al., 2000; Helmstaedter et al., 1998; Martin et al., 1991), which is an arguably unhelpful method of determining domain-specific cognitive impairment (Lezak et al., 2012). Furthermore, research that has administered more comprehensive neuropsychological batteries, has all failed to include measures of attention (Blake et al., 2000; Butler et al., 2009; Butler et al., 2007; Butler et al., 2013). This is surprising considering the prevalence of impairments in attention and processing in people with TLE (Oyegbile et al., 2004) as well as the well-

documented relationship between memory performance and difficulties within this domain (Lezak et al., 2012). It is vital that future research provides more thorough neuropsychological assessment to enable the potentially mediating role of cognitive impairment / between-group difference to be fully considered.

1.3.2.4. Summary

The group study literature builds on single participant research findings. These studies demonstrate evidence of verbal and visual ALF in TLE, investigate the neural basis of this construct (results of which have been arguably inconclusively), and put forward a number of mediating variables.

Findings are largely varied, and interpretations made across research are complicated by differences in design and measures utilised for the assessment of ALF. Furthermore, the majority of group research is flawed in its failure to present single participant data. This has arguably portrayed a certain commonality to the experience of ALF in TLE, which is seemingly questionable (Bell, 2006; Bell et al., 2005). Without single-participant analysis researchers are unable to ascertain the proportion of participants presenting with ALF in their sample, and the presumed inclusion of both affected and unaffected individuals is likely to have diluted the differences observed between groups.

Much of the existing group literature can also be criticised for portraying participants who display more generic encoding, storage and/or recall deficits, when assessed over a standard 30-minute delay, as supportive evidence of ALF when re-assessed over extended delays (Butler et al., 2012; Djordjevic et al., 2011; Helmstaedter et al., 1998). This arguably conflicts with current definitions of ALF (Butler & Zeman, 2008) and adds further ambiguity and uncertainty to what is already a highly contradicted evidence-base. On top of this, many of the published papers have repeatedly re-analysed the same group of TLE participants to draw alternative conclusions (Butler et al., 2009; Butler et al., 2012; Butler et al., 2013; Hoefeijzers et al., 2013), rendering any interpretations highly questionable. Finally, as within the case study literature, very few of the group studies have assessed for impairment across the other domains of cognitive function, which have been documented to impact negatively upon

memory performance (e.g. attention, verbal and visual function; Lezak et al., 2012). It will be important for future research to take these points into consideration if findings in this area are to be furthered.

1.4. Present Study

1.4.1. Rationale & Aims

Research suggests some individuals with TLE experience an accelerated rate of forgetting for new information. This novel phenomenon is referred to as ALF and appears to affect verbal and/or visual memory, on tasks of recall and/or recognition. It has been demonstrated within TLE by both case and group study designs.

People with TLE experiencing ALF appear to be aware of this memory difficulty and often score highly on subjective measures of memory impairment (Butler & Zeman, 2008). However, standard neuropsychological assessment tools appear unable to detect ALF in TLE (Fitzgerald, Mohamed, et al., 2013). This may result from the use of inappropriate testing intervals. The majority of neuropsychological measures assess retrieval from LTM over 30 minutes as standard (Lezak et al., 2012); a timeframe that does not appear sensitive to the effects of ALF (Fitzgerald, Mohamed, et al., 2013). Therefore, despite memory difficulties being widely reported in the TLE population (Butler & Zeman, 2008) it may be that ALF goes largely undiagnosed. This is likely to result in inadequate provision of information, support and/or treatment for those affected.

Despite the above, as yet no specific standardised and/or validated measure exists for the assessment of ALF in TLE. This is arguably exacerbating current clinical issues surrounding the existence, nature and extent of this novel construct.

The absence of specific tools for the assessment of ALF in TLE is arguably also having a detrimental effect on current research and the development of

knowledge within this area. Researchers are relying on a variety of different measures, delivered over a range testing delays and as a result findings are varied with limited potential to draw interpretations across research. Furthermore, much of the available research can be criticised for failing to comprehensively assess for impairment across the other cognitive domains (Bengner et al., 2006; Deak et al., 2011; Jansari et al., 2010; Kemp et al., 2012), rendering it unable to consider the influence of potentially mediating cognitive variables. Additionally, the majority of group-level research has failed to provide single-participant analysis (Butler et al., 2012; Deak et al., 2011; Fitzgerald, Thayer et al., 2013), which has resulted in limited knowledge about the proportion of TLE individuals affected by ALF in each sample. The probable inclusion of both affected and unaffected participants has potentially diluted any differences between groups, and complicated understandings of ALF.

The present study aims to address the issues raised above by adapting subtests from the UK version of an existing and widely-used neuropsychological measure (WMS-IV^{UK}; Wechsler, 2010b) in an attempt to assess its utility with novel procedures at detecting ALF in TLE. The WMS-IV^{UK} has been selected on the following grounds:

- The WMS has historically been the most commonly utilised measure for the assessment of memory difficulties in TLE (Jones-Gotman, 1993). However, as yet there is limited data assessing the validity of its newest edition (WMS-IV) within this population (Loring & Bauer, 2010).

- Although the WMS-III has been used to assess ALF in TLE (Bell, 2006), utility of the WMS-IV has not yet been investigated.

Tests will be adapted to include additional one-week delayed recall and recognition trials. A shorter delay may fail to detect ALF (Bell et al., 2005), whereas any longer could result in floor effects (Muhlert et al., 2011). Alongside measures of memory and ALF, all participants will be administered a comprehensive neuropsychological assessment battery so that the potential

influence of any impairment/s in non-memory cognitive functioning can be considered. Data will be analysed at both the group and individual level.

The present research will be aiming to extend the methods and findings of a previous doctoral research project (Crowley, 2014) in the following ways:

- Recruiting additional TLE and control participants to create a larger and more representative sample.

- Providing additional individual-level analysis, alongside group-level analysis, with the larger sample.

- If necessary, including additional multivariate analysis to consider the influence of between-group differences across all assessed non-memory variables.

1.4.2. Research Questions

Q1: What is the utility of WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction), when adapted to include a one-week testing delay, at detecting ALF in ***a group*** of individuals with TLE compared to a group of unaffected controls?

Q2: What is the influence of non-memory cognitive performance on the presentation and detection of ALF in ***a group*** of individuals with TLE (compared to unaffected controls) when assessed using WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction) with an additional one-week testing delay?

Q3: What is the utility of WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction), when adapted to include a one-week testing delay, at detecting ALF in ***individuals***?

2. METHODS

2.1. Epistemological Position

Epistemology is the branch of philosophy relating to the theory of knowledge (Ferrier, 1854). Multiple different epistemological positions exist (Willig, 2012), each with their own set of assumptions about the construction of knowledge, and the relationship between knowledge and notions of truth, fact, subjectivity and belief (Armstrong, 1973). It is important for researchers to be explicit about their epistemological position (Willig, 2012) as this will influence every aspect of the work from the questions asked, to the chosen methods, analysis and eventual interpretation/s.

Epistemological positions can be largely grouped into the three categories of (1) realist, (2) phenomenological, and (3) social constructionist (Willig, 2012). Realism aims to uncover reliable knowledge from a world that exists independently to the researcher's awareness of it. Realism can be direct; where knowledge is seen as akin to fact and directly mirroring a universal reality, or critical; in which the researcher believes in the existence of a measurable reality but also acknowledges that knowledge is flawed by the imperfections of our attempts to uncover it and influenced by an external social reality. In contrast, phenomenology aims to understand the nature of the participants' subjective reality, as shaped by the researcher's experience. Unlike realism, phenomenology is not interested in the processes underlying participants' experience and therefore no attempts are made to relate this experience to other aspects of "reality" or establish the accuracy of an account. What is of interest is how the participants experience, perceive and interpret an event; and the researcher aims to develop understandings of the world through their participants' eyes. Finally, social constructionism focuses on how reality is constructed socially through the use of language. From this perspective, language and social interaction are understood to mediate human experience. Focus is paid upon the construction of reality through the development /

establishment of social discourse/s and the impact of these discourses upon the experience of individuals.

Within the present research, I have chosen to take an epistemological position of critical realism. In doing so, I attempt to investigate, measure and quantify phenomena (such as “memory” and “forgetting”) within a social and material reality that I believe exists independently of personal experience and across multiple instances in time. From this perspective, a theory-driven approach can be taken and it is hoped that findings will have utility for the assessment of concepts such as ALF in people with TLE in the future. Furthermore, epilepsy is recognised as a physical condition yielding a distinct and qualitatively different neurological profile and set of associated symptoms to that of unaffected persons.

Despite the above, I also believe that concepts such as memory, forgetting and ALF are not ‘real’, physical entities but socially constructed categories, and that perceptions of ‘normal’ in relation to cognitive performance fluctuate over time and are dependent upon socio-political, historical and cultural contexts (Flynn, 1987). I do not believe my attempts to measure and/or quantify these constructs will mirror reality or absolute truth; instead they will be indirect, inferred and interpreted within the present context. Even the medical diagnoses I grapple with can be challenged; and it is acknowledged that the classification of epilepsy has been open to much debate, criticism and variance over the years (Scambler, 1989). From this position, I believe nothing can be taken for granted, knowledge is fallible and cannot be aligned with fact, and findings must be interpreted tentatively with an awareness of their limitations and boundaries.

2.2. Ethics

The present research was registered with and ethically approved by the University of East London (Appendix 3 & 4). NHS ethics was granted from the Camden & Islington branch of the National Research Ethics Committee (Appendix 5) and Research and Development approval was gained from Barts

Health Research Joint Management Office (Appendix 6). Permission was also gained from the Consultant Neurologist at the Royal London Hospital (RLH) to recruit from his patients and from Epilepsy Action (EA) to recruit through their organisation. All participants gave fully informed consent (Appendix 7, 8 & 9).

2.3. Design

A cohort design was employed to compare the performance of TLE participants with unaffected (typically-developed neurologically intact) controls on the three WMS-IV^{UK} subtests of (1) Logical Memory, (2) Verbal Paired Associates, and (3) Visual Reproduction, which were adapted to include an additional one-week testing delay. It was necessary to use a control group, as there is currently no available normative data for the WMS-IV^{UK} procedures, when adapted to include an additional delayed recall / recognition trial.

The investigated predictor variable was diagnosis, with two levels of (1) TLE versus (2) unaffected control (between-subjects). The evaluated outcome variables were participants' recall and recognition performance on WMS-IV^{UK} subtests of (1) Logical Memory, (2) Verbal Paired Associates and (3) Visual Reproduction, assessed at the three time points of (1) immediate, (2) 30-minute delay, and (3) one-week delay.

Quantitative methods of data analysis were utilised.

2.4. Participants

2.4.1. TLE Group

Additional TLE participants were recruited to add to the existing TLE data collected by Crowley (2014). TLE participants were recruited from two sources: the neurology department of the RLH (Barts and the London NHS Trust) and EA. Participants were required to have a diagnosis of TLE, confirmed by a

neurologist. They were also required to be within the age range of the normative data sample for all assessment tools utilised (18-69 years).

2.4.1.1. Royal London Hospital

The RLH was an existing recruitment site, also utilised to recruit TLE participants within the original study (Crowley, 2014). Suitable participants were identified by the Consultant Neurologist and invited to participate in the present research as part of their standard neuropsychological assessment. Epilepsy diagnoses were confirmed by clinical judgement of the Consultant Neurologist; where possible supported by electroencephalography (EEG) and/or magnetic resonance imaging (MRI) data. See Appendix 10 for a copy of the RLH invitation letter.

2.4.1.2. Epilepsy Action

EA is a UK registered charity providing support and information for people with epilepsy. This comprised an entirely novel recruitment site, which was not utilised by the original study (Crowley, 2014). Participants with a diagnosis of TLE were recruited through advertisements that were placed on the website and distributed to local support groups. See Appendix 11 and 12 for a copy of the EA advertising leaflet and invitation letter.

2.4.2. Control Group

Additional control participants were recruited to add to the existing control data via opportunity sampling to achieve a convenience sample. As demographic variables have been shown to strongly affect performance on neuropsychological measures (Lezak et al., 2012) attempts were made to match the control group to the TLE group in terms of age, gender and educational opportunity. As with the TLE group, control participants were also required to fall within the age range of the normative data sample for all utilised assessment tools (18-69 years). See Appendix 13 for a copy of the control group invitation letter.

2.4.3. Exclusion Criteria

Research suggests a range of physical and psychological variables that impact upon neuropsychological test performance (Lezak et al., 2012). The following were applied as exclusion criteria for both the TLE and control group:

- Non-fluent in English (Lezak et al., 2012)
- Experience of seizure/s within 24 hours prior to testing (O'Connor et al., 1997)
- Epilepsy surgery (Sherman et al., 2011)
- Co-morbid neurological disorders known to affect cognitive functioning (assessed on a case-by-case basis)
- Diagnosed learning disabilities (Lezak et al., 2012)
- Significant head injury in the previous ten years (Kinnunen et al., 2010)
- Significant sensory difficulties (e.g. in vision or hearing; Lezak et al., 2012)
- Psychiatric diagnosis (Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lönnqvist, 2008)
- Current substance misuse (Rogers & Robbins, 2001)
- Any other physical / psychological difficulties known to significantly affect performance on neuropsychological assessment (reviewed on a case-by-case basis)

2.5. Procedures

2.5.1. Screening

All referred / interested participants were invited for an initial screening appointment, during which they were provided with any further information about the research that they asked about and fully informed consent was obtained. Suitability to participate in the study was assessed in terms of the exclusion criteria outlined above. The following information was also recorded, to address any potentially confounding variables on test performance:

- Demographic Information (Lezak et al., 2012)
    - Age, gender, ethnicity, education and occupation
- Epilepsy details (for TLE group only) (Aldenkamp & Arends, 2004)
    - Epilepsy type, seizure type, seizure onset site, seizure frequency (current and historical), aetiology (if known), age of onset
- Physical and mental health (Castaneda et al., 2008)
- Current medication (Stewart, 2005)
- Current substance use (Rogers & Robbins, 2001)
- Recent life events (Vedhara, Hyde, Gilchrist, Tytherleigh, & Plummer, 2000)

TLE patients who did not meet the inclusion criteria or declined to participate in the research were still offered a full neuropsychological assessment to ensure equal provision of care and ethical integrity.

2.5.2. Assessment

Suitable participants were invited to attend an initial (T1) and one-week follow-up (T2) testing appointment. At T1, participants were asked to complete a neuropsychological assessment battery, developed specifically for the present research. Included in this battery were the three to-be-investigated memory subtests from the WMS-IV^{UK}, alongside measures of attention/processing, language, visuospatial, and executive function (see Section 2.6. Measures). It was necessary to administer a comprehensive neuropsychological test battery to control for impairment in any of these interacting cognitive domains (Lezak et al., 2012). Administration manuals were followed precisely in the delivery of all measures to support reliability and attempts were made to ensure an optimal working environment (quiet, free from distraction, well lit and with no other people present during the testing). The assessment took two hours on average and included a 20-minute break. More regular / longer breaks were offered if necessary / requested. TLE participants who experienced seizures within 24 hours of the initial testing appointment were re-scheduled, as research has demonstrated declined levels of cognitive function during this period (O'Connor et al., 1997).

Between sessions, participants were asked to complete several self-report questionnaires assessing mood, sleep and subjective memory functioning (see Section 2.6. Measures). TLE participants were also asked to record any seizures they experienced between the two appointments. Participants were not given any specific information about the tests they would be completing at T2 in order to prevent the conscious rehearsal of material between sessions.

Upon returning at T2, participants were re-administered the adapted WMS-IV^{UK} subtests (see Section 2.6. Measures). At this appointment, TLE participants were also provided with verbal feedback and a report summarising their results from the previous session, including areas of relative strength, weakness and recommendations. A copy of this report was forwarded to participants' Consultant Neurologist / GP, with consent.

Supervision, advice and consultation were provided throughout from the Director of Studies to ensure the appropriate administration, scoring and interpretation of assessments.

2.6. Measures

2.6.1. Neuropsychological Test Battery

The following neuropsychological test battery was developed; and comprised measures of memory, attention/processing, language, visuospatial and executive function within both verbal and visual domains. A measure of premorbid ability was also included to enable the researcher to differentiate areas of cognitive decline from pre-existing cognitive function. Attempts were made to include measures from commonly used and robust test batteries, which have been standardised on large samples and are regarded as both valid and reliable measures of their intended constructs within the literature. In test batteries with several editions, the newest available version was always included and where available, UK tests were utilised. See Table 1 for an overview of measures used, validity and reliability evidence.

Table 1

Utilised Neuropsychological Assessment Tools, Reliability and Validity Evidence

Instrument	**Subtest/s**	**Evidence of Reliability and Validity**
Test of Premorbid Functioning - (TOPF^{UK}; Wechsler, 2011)	NA	Wechsler (2011)
Wechsler Adult Intelligence Scale - Fourth UK Edition (WAIS-IV^{UK}; Wechsler, 2010a)	Symbol Search Digit Span Forwards Digit Span Backwards Digit Span Sequencing Similarities Visual Puzzles	Wechsler (2010a); Benson, Hulac, & Kranzler (2010); Canivez & Watkins (2010); Hartman (2009); Holdnack, Zhou, Larrabee, Millis, & Salthouse (2011)
Wechsler Memory Scale - Fourth UK Edition (WMS-IV^{UK}; Wechsler, 2010b)	Logical Memory Verbal Paired Associates Design Memory Visual Reproduction Spatial Addition Symbol Span	Wechsler (2010b); Hoelzle, Nelson, & Smith (2011); Holdnack, Zhou, Larrabee, Millis, & Salthouse (2011)
Delis-Kaplan Executive Function System (DKEFS; Delis, Kaplan, & Kramer, 2001)	Verbal Fluency	Delis, Kaplan, & Kramer (2001); Delis, Kramer, Kaplan, & Holdnack (2004); Homack, Lee, & Riccio (2005); Shunk, Davis, & Dean (2006)
Hayling and Brixton Tests (Burgess & Shallice, 1997)	Brixton Spatial Anticipation	Burgess & Shallice (1997); Crawford & Henry (2005); de Frias, Dixon, & Strauss (2006); Odhuba, Broek, & Johns (2005); Wood & Liossi (2006)

2.6.1.1. Premorbid Ability - TOPF^{UK} (Wechsler, 2011)

Within this test participants are administered 70 irregular words (atypical grapheme-to-phoneme pronunciation), which they are required to accurately read aloud to provide an estimate of vocabulary. Vocabulary has been shown to be relatively resistant to cognitive decline (Nelson, 1981) and can be compared to the normative data in order to gain an estimate of premorbid cognitive functioning. Test manual confidence intervals suggest TOPF estimated premorbid ability correlates well with measures of general verbal function (Wechsler, 2011), and research suggest a positive relationship between measures of premorbid ability and memory, especially within the verbal modality (Lezak et al., 2012). In contrast, wide test manual confidence intervals intimate the TOPF$^{UK's}$ limited ability to provide accurate estimates of premorbid processing speed (Wechsler, 2011).

2.6.1.2. Processing Speed - WAIS-IV^{UK} Coding (Wechsler, 2010a)

Participants are required to select and enter as many symbols as possible into their corresponding digit boxes within a two-minute time limit, using a visual key. Demand is placed on visuo-motor processing speed, as well as visual perception and analysis.

2.6.1.3. Attention (Short-Term Stores & Working Memory)

2.6.1.3.1. WAIS-IV^{UK} Digit Span Forwards (Wechsler, 2010a)

This subtest assesses auditory attention span. Participants are required to listen to and immediately repeat random digit strings, which increase in length as they progress through the task.

2.6.1.3.2. WAIS-IV^{UK} Digit Span Backwards (Wechsler, 2010a)

This subtest was used as a measure of auditory/verbal working memory. Participants are verbally presented with a string of random digits, which they are required to immediately repeat back to the examiner in reverse order.

2.6.1.3.3. WAIS-IV^{UK} Digit Sequencing (Wechsler, 2010a)

This comprised a second measure of auditory/verbal working memory. Within this subtest participants are again presented with a verbal string of random digits. However, this time they are required to repeat in numerical order.

2.6.1.3.4. WMS-IV^{UK} Symbol Span (Wechsler, 2010b)

This subtest assesses visuospatial span and visual working memory. Participants are briefly presented with a series of symbols. They are then asked to select the correct symbols in their correct order from a subsequently presented page of the stimulus book. The number of symbols presented increases as the participant progresses through the task.

2.6.1.3.5. WMS-IV^{UK} Spatial Addition (Wechsler, 2010b)

This subtest provides a measure of visuospatial working memory. Participants are briefly presented with two grids of red and blue circles, one after the other. They are then required to reproduce an amalgamated version of these two grids, using the provided blue and white disks and adhering to a series of rules.

2.6.1.4. Verbal Function - WAIS-IV^{UK} Similarities (Wechsler, 2010a)

This subtest provides a measure of abstract verbal reasoning. Participants are verbally presented with two different words and required to describe how they are alike.

2.6.1.5. Visuospatial Function - WAIS-IV^{UK} Visual Puzzles (Wechsler, 2010a)

This subtest provides a measure of visuospatial reasoning. Participants are required to recreate a picture using three of six presented visual puzzle pieces.

2.6.1.6. Executive Functioning

2.6.1.6.1. DKEFS Verbal Fluency (Delis et al., 2001)

This subtest provides a measure of verbal executive function, via letter and category fluency as well as category switching. Within the first part of this test participants are presented with a given letter (“F”, then “A” and then “S”) and required to verbalise as many words as possible beginning with that letter within

a one-minute timeframe. After this, participants are asked to do the same with categories ("animals" and "boys'/men's names"). The final task requires participants to verbally generate and alternate between two categories ("fruit" and "furniture").

2.6.1.6.2. Brixton Spatial Anticipation (Burgess & Shallice, 1997)

This subtest provides a measure of visuospatial executive functioning, and places demand on planning, rule acquisition and switching. Participants are presented with one blue circle and a series of 10 spatial locations. They are required to ascertain and apply a variable rule in order to predict the subsequent spatial location of the black dot.

2.6.1.7. Learning & Memory

The following subtests were administered from the WMS-IV^{UK} (Wechsler, 2010b) as measures of immediate and delayed verbal and visual memory.

2.6.1.7.1. Logical Memory

This subtest provides an assessment of both immediate and delayed verbal (semantic-episodic) memory for two short stories, which are presented verbally. Participants' ability to both freely recall (in the immediate and delayed phases) and recognise information from the stories using a series of yes/no questions (in the delayed phase only) is assessed.

2.6.1.7.2. Verbal Paired Associates

Immediate and delayed verbal (material-specific) memory for associated word pairs is assessed within this subtest. Participants are presented with 14 novel word pairs over four separate trials. After the administration of each trial, cued recall is assessed and feedback is given. Cued recall (without feedback) and recognition are re-assessed after a 30-minute delay.

2.6.1.7.3. Visual Reproduction

Visual memory for a set of five novel designs is assessed by this subtest. Participants are presented with five novel designs, in sequential order, for a period of 10 seconds each. After the presentation of each design, participants'

visual recall is assessed via their ability to draw the design. Recall is reassessed after a 30-minute delay. Participants' visual recognition of each original design, when presented alongside five novel designs, is also assessed at this delayed testing phase.

2.6.1.8. Extended Delay Trials

The delayed recall and recognition phases of WMS-IV^{UK} subtests (1) Logical Memory, (2) Visual Reproduction, and (3) Verbal Paired Associates were re-administered after a one-week delay as measures of verbal and visual extended memory retrieval. Subtests were re-administered in the advised sequential order and the wording of instructions was kept as close as possible to the original script. It was necessary to make some minor changes to the wording, for example "earlier" was substituted for "last week", to ensure that instructions still made sense when administered in the context of a one-week delay (see Appendix 14, 15 & 16).

2.6.1.9. Questionnaires

Self-report questionnaire measures of mood and sleep were administered to control for difficulty in either of these areas, both of which have been associated with subjective impairments in cognitive function (Castaneda et al., 2008; Durmer & Dinges, 2005). Furthermore, as research suggests a relationship between self-reported memory difficulties and ALF in TLE (Butler et al., 2009), questionnaire measures of memory were also included.

2.6.1.9.1. Mood

The Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) was used to assess for symptoms of anxiety and/or depression. This measure requires participants to rate how far they agree with a series of fourteen statements, when considered over the past week. The HADS was initially developed as a screening tool for use in a hospital setting, but research since suggests its validity when administered in the community and primary care settings (Snaith, 2003). It is now widely used in neuropsychological research and practice (McGuire, Murray, & Shah, 1993; Muslimović, Post, Speelman, & Schmand, 2005; Simioni et al., 2010).

Unlike Beck's Anxiety / Depression Inventories (Beck & Steer, 1990; Beck, Steer, & Brown, 1996), the HADS does not include any somatic items, making it more appropriate for people with physical health difficulties (Zigmond & Snaith, 1983). Furthermore, it is a lot quicker to administer than many of the more commonly utilised measures (Beck & Steer, 1990; Beck, Steer, & Brown, 1996).

2.6.1.9.2. Sleep

The Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989) was used as a measure of sleep. This nineteen-item measure was developed to assess sleep quality and disturbance. Participants are required to rate how far they agree with each statement over the past month, in order to generate seven sub-scale scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, daytime dysfunction) and one global score. The PSQI is suggested to have good utility in both research and clinical practice (Buysse et al., 1989). Although a myriad of sleep measures exist, the PSQI is one of the quicker to administer and most widely used in epilepsy research (Carrion, Nunes, Martinez, Portuguez, & da Costa, 2010; Chen et al., 2011; Krishnan et al., 2012).

2.6.1.9.3. Subjective Memory Function

The Everyday Memory Questionnaire - Revised (EMQ-R; Royle & Lincoln, 2008) was used as a measure of subjective memory function. In this questionnaire participants are asked to estimate the frequency of 18 everyday memory difficulties, on a scale of zero to five, over the past month. Unlike many of the other measures of subjective memory function, the EMQ is the only tool validated by research investigating ALF in TLE (Butler et al., 2009).

2.7. Participant Characteristics

A total of 51 (25 TLE; 26 control) participants were assessed. 30 participants were recruited and assessed by the previous researcher (Researcher 1) and assistant (Research Assistant) during the initial phase of this study. The remaining 21 participants were recruited and assessed by the present researcher (Researcher 2). Of the TLE participants, 19 were recruited through the RLH and the remaining 6 were recruited through EA. See Table 2 for a summary of assessments completed by each researcher.

Table 2

Summary of Assessments Completed by Researcher and Recruitment Site

Researcher	**Control Participants**	**TLE Participants**	
		RLH	**EA**
Researcher 1	13	8	0
Research Assistant	3	6	0
Researcher 2	10	5	6

A summary of participant demographics in terms of gender and ethnicity is provided in Tables 3 and 4 overleaf. Further demographic information is provided in Section 3.2.

Table 3

Gender Frequencies

Group	Gender Frequency (Proportion)	
	Female	**Male**
TLE	13 (0.52)	12 (0.48)
Control	13 (0.50)	13 (0.50)
Total	26 (0.51)	25 (0.49)

Pearson's chi-square suggests gender to be well matched between groups, $\chi^2(1)=0.02$, phi=-.02, p=.99.

Table 4

Ethnicity Frequencies

Group	Ethnicity Frequency (Proportion)						
	A	**B**	**C**	**D**	**E**	**F**	**G**
TLE	20 (0.80)	0 (0.00)	1 (0.04)	1 (0.04)	3 (0.12)	0 (0.00)	0 (0.00)
Control	19 (0.73)	1 (0.04)	2 (0.08)	1 (0.04)	0 (0.00)	1 (0.04)	2 (0.08)
Total	39 (0.77)	1 (0.02)	3 (0.06)	2 (0.04)	3 (0.06)	1 (0.02)	2 (0.04)

A=White British; B=White Irish; C=Black British; D=Black Caribbean; E=Indian; F=Sri Lankan; G=White Other

A summary of TLE participants' epilepsy characteristics is provided in Table 5 overleaf.

Table 5

TLE Group Epilepsy Characteristics

No.	Age (years)	Seizure Laterality*	Seizure Type/s	Age of Onset (years)	Duration (years)
1	34	Right	CPS, SPS, GTCS	29	5
2	49	Left	CPS	15	35
3	34	N/K	CPS, GTCS	13	21
4	49	Left	CPS	35	14
5	23	N/K	SPS, GTCS	20	3
6	31	Left	CPS, SPS, GTCS	14	17
7	32	Left	SPS, GTCS	13	19
8	21	Left	SPS	13	8
9	47	N/K	SPS, GTCS	44	3
10	23	Left	CPS, GTCS	23	0
11	26	Left	CPS, GTCS	24	2
12	49	Left	SPS, CPS	37	12
13	19	Right	SPS, CPS	18	1
14	24	Left	SPS, GTCS	24	0
15	19	Left	CPS, GTCS	15	4
16	32	N/K	SPS	3	29
17	70	Left	CPS, SPS	68	2
18	49	N/K	CPS, SPS	12	37
19	57	Left	SPS	18	39
20	58	Right	CPS, GTCS	5	53
21	25	Right	CPS	15	10
22	25	Right	CPS, GTCS	8	17
23	54	N/K	CPS	15	39
24	33	N/K	CPS, GTCS	0	33
25	43	Left	GTCS	40	3

*CPS=complex partial seizure; GTCS=generalised tonic-clonic seizure; N/K=not known; SPS=simple partial seizure; *laterality confirmed by EEG or MRI*

3. RESULTS

3.1. Methods of Analysis

Assessments were scored in accordance with published test criteria, and age-scaled and/or standardised scores were calculated where available. See Appendix 17 for a summary of scores derived from each variable for analysis.

Data was analysed using SPSS (Statistical Package of Social Sciences) for Macintosh, Version 20. Analysis procedures are described below:

a) Initial boxplots and histograms were generated and checked to identify outliers. Coding errors were corrected.

b) Exploratory data analysis was conducted across all variables and violations to the parametric assumptions were examined (skewness>1; kurtosis>3). Shapiro-Wilk's test was used to investigate normality of distributions. Results were interpreted conservatively at a significance level of $p \leq 0.01$, and in conjunction with histogram, boxplot and normal Q-Q plot data.

c) One-Way Analysis of Variance (ANOVA) was used to assess for between-group differences on all variables and effect sizes were calculated (Eta [η]). ANOVA has been shown to reduce Type 1 error in multiple testing (Bender & Lange, 2001) and is robust in skewed distributions (Glass, Peckham, & Sanders, 1972) where group size is equal (Lunney, 1970). Homogeneity of variance was assessed using Levene's test and Brown-Forsythe's correction applied where this assumption was violated.

d) Kolmogorov-Smirnov's test was utilised to assess for instances where control group performance deviated from the typical. The performance of both groups was compared with population age-scaled norms (M=10; SD=3) for each of the cognitive measures from T1, with the exception of the recognition memory tasks for which normative age-scaled scores do not exist.

e) General Linear Model (GLM) analysis was conducted on each of the WMS-IV^{UK} subtests administered to assess ALF where between-group differences were found. Non-memory variables with significant between-group differences were assessed for co-linearity using Spearman's Rho, and distinct variables considered within the multivariate GLM as covariates. Parametric assumptions of the multivariate GLM (normality of residuals, homogeneity of error variances) were assessed using Shapiro-Wilk's and Levene's tests alongside histogram, box- and normal Q-Q plots.

f) Impaired individual scores (defined as ≤2 SDs from the control group mean; Armstrong & Morrow, 2010) on each of the WMS-IV^{UK} subtests administered to assess ALF were noted. Impaired individual scores on non-memory cognitive (≤2 SDs from the control group mean) and non-cognitive (≥2 SDs from the control group mean) variables were also recorded for participants displaying impaired memory performance solely at the extended delay.

Significance of the p-value was set to $p<0.05$ (Bennett & Fisher, 1995) and effect sizes were interpreted in line with Cohen (1992). Due to the relatively small sample size, limitations of the p-value/significance testing (Johnson, 1999) and current move away from reporting statistical significance in psychological research (APA, 2009), focus is placed on effect size ($\eta>.3$; Cohen, 1992) as an indicator of between-group difference where these values (p versus η) contrast.

Data that fell outside of the original protocol and procedures taken are described below:

- One TLE participant turned 70-years-old between screening and T1. This data was included and age-scaled using 65-69-year-old norms to sustain transformation consistency.

- Instances of missing data are detailed below. Participants with missing data were omitted from the multivariate GLM analysis only.

- One TLE participant was unable to return for T2 so completed the extended recall and recognition elements of Verbal Paired Associates and Logical Memory over the telephone. Due to the visual nature of the Visual Reproduction task, the extended delay phase of this subtest was omitted.

- There was one missing TLE PSQI score from the original dataset.

3.2. Demographics

3.2.1. Exploratory Data Analysis

A summary of participant demographics (age, education, TOPF estimated premorbid ability) is provided in Table 6. Taken together, results of Shapiro-Wilk's test and plotted data suggest normality is upheld for the majority of distributions, except 'age', where a higher number of younger participants cause positive skew across both groups (see Appendix 19 for histograms).

Table 6

Descriptive Statistics for Participant Demographics

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
Age (years)	**TLE***	37.04	14.33	19	70	0.57	-0.68	.05
	Control*	36.15	13.52	18	66	0.81	-0.49	.01
Education (years)	**TLE**	13.64	2.41	10	18	0.46	-0.99	.02
	Control	13.42	3.13	6	19	-0.16	-0.32	.36
TOPF Estimated Ability	**TLE**	97.84	9.03	75	119	0.06	1.64	.14
	Control	97.73	9.67	78	116	0.15	-0.03	.18

**non-normal distribution*

3.2.2. Group Comparisons

Assumptions of homogeneity of variance are upheld; Levene's test failed to find a significant difference between groups on variables of age, $F(1,49)=0.18$, p=.67, education, $F(1,49)=1.77$, p=.19, or TOPF estimated premorbid ability, $F(1,49)=0.62$, p=.44.

Examination of the means (Table 6) does not indicate any between-group differences on the demographic variables. In line with this, ANOVA does not suggest any statistically significant differences in age, $F(1,49)=0.05$, η=.03, p=.82, education, $F(1,49)=0.08$, η=.04, p=.78, or TOPF estimated premorbid ability, $F(1,49)=0.00$, η=.01, p=0.97. Results suggest groups are well matched across the demographic variables.

3.3. Mood, Sleep and Subjective Memory Function

3.3.1. Exploratory Data Analysis

A summary of scores for subjective measures of mood (HADS), sleep quality (PSQI) and memory function (EMQ) is provided in Table 7. Taken together, results of Shapiro-Wilk's test and plotted data suggest the TLE group PSQI distribution violates assumptions of normality; several higher scoring outliers produce positive skew and high kurtosis. The control group HADS Depression distribution also appears non-normal, with a large number of low scoring participants again producing positive skew and high kurtosis. See Appendix 19 for histograms.

3.3.2. Group Comparisons

Levene's test suggests the homogeneity of variance assumption is violated for the EMQ, $F(1,49)=8.82$, p=.01. In comparison, this assumption is upheld for the PSQI, $F(1,48)=2.16$, p=.15, HADS Anxiety, $F(1,49)=1.98$, p=.17, and HADS Depression, $F(1,49)=2.46$, p=.12, scales.

Examination of the means (Table 7) suggests TLE participants scored higher than controls on all four measures (on which higher scores denote a higher level of difficulty). This is reflected in the analysis and ANOVA / Eta both suggest the TLE group scored significantly higher than controls on the EMQ, $F(1,26)=62.73$, $\eta=.75$, $p=.00$ (Brown-Forsythe's correction was applied), PSQI, $F(1,48)=9.00$, $\eta=.40$, $p=.00$, HADS Anxiety, $F(1,49)=12.67$, $\eta=.45$, $p=.00$, and HADS Depression, $F(1,49)=15.17$, $\eta=.49$, $p=.00$, scales.

Table 7

Descriptive Statistics for Mood, Sleep and Subjective Memory Function

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
EMQ	**TLE**	24.00	8.90	11	43	0.39	-0.60	.43
	Control	8.15	4.66	1	17	0.66	-0.45	.05
PSQI**	**TLE***	7.64	5.11	1	25	2.12	5.49	.00
	Control	4.24	2.45	1	10	0.60	0.01	.12
HADS Anxiety	**TLE**	9.44	4.34	1	18	0.04	-0.69	.87
	Control	5.54	3.46	0	12	0.15	-0.99	.27
HADS Depression	**TLE**	6.24	3.68	0	13	0.19	-0.82	.55
	Control*	2.62	2.94	0	13	1.91	5.17	.00

**non-normal distribution; **data based on 24/25 TLE participants*

3.4. Non-Memory Cognitive Functions

3.4.1. Exploratory Data Analysis

A summary of participants' age-scaled scores for all non-memory measures of cognitive function is provided in Table 8. Taken together, Shapiro-Wilk's test and the data plots suggest assumptions of normality are upheld for the majority of distributions. This is with the exception of the control group's Brixton Spatial Anticipation scores, which have negative skew caused by a large number of high scoring participants (see Appendix 19 for histogram).

3.4.2. Group Comparisons

Levene's test suggests homogeneity of variance is upheld for all non-memory cognitive variables. From examining the means (Table 8) it appears that control participants achieved higher scores on all measures. ANOVA suggests this difference to be statistically significant, with a medium/large effect size, for tasks of semantic fluency (Category Fluency, Switch Accuracy, Switch Total). A difference approaching statistical significance, with an effect-size approaching medium, was also observed for the Visual Puzzles task. See Table 9.

Kolmogorov-Smirnov's test suggests control participants performed significantly higher than expected from a normative sample (M=10; SD=3) on tasks of visuospatial and executive function. In comparison, the TLE group performed significant lower than population norms on tasks of processing speed and semantic fluency. See Table 10.

Table 8

Descriptive Statistics for Tasks of Non-Memory Cognitive Function

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WAIS Similarities	**TLE**	8.96	2.88	3	15	0.10	0.03	.78
	Control	10.12	2.57	4	15	-0.48	0.63	.22
WAIS Visual Puzzles	**TLE**	9.80	2.93	5	15	0.41	-0.97	.10
	Control	11.42	2.94	6	16	-0.21	-0.89	.29
WAIS Digit Span	**TLE**	8.48	2.65	4	13	-0.07	-1.02	.37
	Control	9.58	2.85	5	18	0.88	1.88	.16
WAIS Coding	**TLE**	8.96	2.26	4	14	0.43	0.93	.08
	Control	9.88	2.76	6	17	0.92	0.84	.05
WMS Symbol Search	**TLE**	9.60	2.53	4	15	0.21	0.20	.52
	Control	10.92	2.68	5	15	-0.32	-0.65	.43
WMS Spatial Addition	**TLE**	10.16	3.18	3	14	-0.88	0.14	.02
	Control	10.62	3.05	4	17	-0.03	-0.25	.76
DKEFS Letter Fluency	**TLE**	9.76	3.88	3	16	0.17	-1.11	.23
	Control	11.73	3.75	3	19	-0.04	0.53	.50
DKEFS Category Fluency	**TLE**	8.88	3.59	2	16	-0.10	-0.49	.78
	Control	12.81	4.02	4	19	-0.67	0.14	.17
DKEFS Switch Total	**TLE**	8.64	2.72	4	14	-0.05	-0.48	.30
	Control	11.88	3.00	5	17	-0.59	0.27	.06
DKEFS Switch Accuracy	**TLE**	9.80	2.18	6	14	0.20	-0.70	.28
	Control	12.35	2.71	6	17	-0.42	0.16	.46
Brixton Spatial Anticipation	**TLE**	11.00	3.50	2	16	-0.81	0.41	.20
	Control*	11.31	2.95	3	15	-1.31	1.46	.00

**non-normal distribution*

Table 9

Between-Group Comparisons for Tasks of Non-Memory Cognitive Function

	Homogeneity of Variance		ANOVA		Measures of Association	
	F	**Sig.**	**F**	**Sig.**	**η**	**η^2**
WAIS Similarities	0.54	.46	2.29	.14	.21	.05
WAIS Visual Puzzles	0.06	.81	3.90	.05	.27	.07
WAIS Digit Span	0.05	.82	2.03	.16	.20	.04
WAIS Coding	1.10	.30	1.70	.20	.18	.03
WMS Symbol Search	0.38	.54	3.28	.08	.25	.06
WMS Spatial Addition	0.00	.97	0.27	.60	.07	.01
DKEFS Letter Fluency	0.68	.41	3.41	.07	.26	.07
DKEFS Category Fluency	0.06	.80	13.52	.00*	.47**	.22
DKEFS Switch Total	0.00	.99	16.34	.00*	.50**	.25
DKEFS Switch Accuracy	0.63	.43	13.59	.00*	.47**	.22
Brixton Spatial Anticipation	0.61	.44	0.12	.74	.05	.00

**p<.05; **η>.3*

Table 10

Kolmogorov-Smirnov Comparisons between Population Norms and TLE / Control Group Non-Memory Cognitive Performance

	TLE Group		Control Group	
	Stat.	**Sig.**	**Stat.**	**Sig.**
WAIS Similarities	1.15	.14	1.37	.18
WAIS Visual Puzzles	0.95	.32	1.46	.03*
WAIS Digit Span	1.35	.05	0.98	.29
WAIS Coding	1.90	.00*	1.06	.21
WMS Symbol Search	0.90	.39	1.01	.21
WMS Spatial Addition	1.10	.18	1.01	.21
DKEFS Letter Fluency	0.94	.34	1.46	.03*
DKEFS Category Fluency	1.14	.15	2.44	.00*
DKEFS Switch Total	1.55	.02*	2.24	.00*
DKEFS Switch Accuracy	0.90	.39	2.24	.00*
Brixton Spatial Anticipation	1.35	.05	2.05	.00*

**p<.05*

3.5. Memory Function - Standard Trials

3.5.1. Exploratory Data Analysis

A summary of participants' scores on all standard measures of memory function is provided in Table 11. Age-scaled scores are provided for all variables apart from the recognition tasks, where the manual provides cumulative percentile ranges. As SPSS does not accept score ranges, these are reported in ranked order from one to seven (see Appendix 18). Within this context "delayed" refers to the standard 30-minute delay trials.

Taken together, results of Shapiro-Wilk's test and the data plots suggest the majority of distributions meet assumptions of normality. This is with the exception of the delayed recognition tasks, in which superior scores (across both groups) result in negative skew and high kurtosis (see Appendix 19 for histograms). Limitations of the ranking system used to convert these scores (with unequal score distribution between ranks) may have contributed to this profile: these results are interpreted with caution.

3.5.2. Group Comparisons

Levene's test suggests homogeneity of variance is violated for the majority (5/8) of variables. From analysing the means, it appears control participants scored higher on all measures. Eta suggests a medium/large between-group difference for all three phases of Verbal Paired Associates (VPA). A medium and large effect of group are also seen for delayed recall of Logical Memory (LM) and Visual Reproduction (VR) respectively. Between-group differences for VR delayed recognition are approaching medium effect. In line with Eta, ANOVA (with Brown-Forsythe's correction applied where relevant) suggests control participants performed significantly higher on each of the above variables with the exception of LM. See Table 12.

Table 11

Descriptive Statistics for Tasks of Memory Function

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WMS LM Immediate Recall	**TLE**	9.80	3.23	3	15	-0.53	-0.56	.27
	Control	11.27	2.74	4	15	-0.99	0.82	.06
WMS LM Delayed Recall	**TLE**	8.92	3.56	2	15	-0.20	-0.08	.33
	Control	11.00	2.80	3	15	-0.94	1.52	.08
WMS LM Delayed Recog.	**TLE***	5.24	1.90	1	7	-0.85	-0.50	.00
	Control*	5.96	1.15	3	7	-0.95	0.22	.00
WMS VPA Immediate Recall	**TLE**	7.92	2.52	3	14	0.15	0.38	.69
	Control	10.50	2.37	6	17	0.50	1.13	.48
WMS VPA Delayed Recall	**TLE**	7.72	2.81	1	13	-0.52	0.53	.15
	Control	11.08	2.28	5	15	-0.72	0.80	.29
WMS VPA Delayed Recog.	**TLE**	4.36	1.75	1	7	0.10	-0.82	.03
	Control*	6.00	1.23	3	7	-0.97	-0.18	.00
WMS VR Immediate Recall	**TLE**	10.24	2.57	4	14	-0.63	-0.05	.23
	Control	11.46	2.10	6	15	-0.56	0.42	.30
WMS VR Delayed Recall	**TLE**	9.52	2.79	5	17	0.63	0.72	.30
	Control	12.65	2.76	7	17	-0.14	-0.88	.37
WMS VR Delayed Recog.	**TLE***	5.16	1.91	1	7	-0.76	-0.54	.00
	Control*	6.08	1.13	2	7	-1.97	5.73	.00

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *non-normal distribution*

Table 12

Between-Group Comparisons for Tasks of Memory Function

	Homogeneity of Variance		ANOVA		Brown-Forsythe		Measures of Association	
	F	Sig.	F	Sig.	Stat.	Sig.	η	η^2
WMS LM Immediate Recall	2.80	.02*			3.06	.09	.24	.06
WMS LM Delayed Recall	1.79	.11	0.65	.86			.32**	.10
WMS LM Delayed Recog.	1.21	.33	0.62	.88			.23	.05
WMS VPA Immediate Recall	7.17	.00*			14.19	.00*	.47**	.23
WMS VPA Delayed Recall	3.04	.01*			21.89	.00*	.56**	.31
WMS VPA Delayed Recog.	2.02	.07	0.56	.93			.48**	.24
WMS VR Immediate Recall	1.53	.18	1.05	.46			.26	.07
WMS VR Delayed Recall	3.30	.01*			16.30	.00*	.50**	.25
WMS VR Delayed Recog.	2.65	.02*			4.32	.04*	.29	.08

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05; **η>.3*

Kolmogorov-Smirnov's test suggests control participants performed significantly higher than expected from a normative sample (M=10; SD=3) on the immediate and delayed recall phases of LM and VR, and on the delayed recall phase of VPA. In comparison, TLE participants performed significant lower than population norms on the immediate and delayed VPA recall trials. See Table 13.

Table 13

Kolmogorov-Smirnov Comparisons between Population Norms and TLE / Control Group Standard Memory Performance

	TLE Group		**Control Group**	
	Stat.	**Sig.**	**Stat.**	**Sig.**
WMS LM Immediate Recall	0.74	.65	1.65	.01*
WMS LM Delayed Recall	1.15	.14	1.45	.03*
WMS VPA Immediate Recall	1.95	.00*	1.01	.18
WMS VPA Delayed Recall	2.01	.00*	1.57	.02*
WMS VR Immediate Recall	0.95	.32	1.84	.01*
WMS VR Delayed Recall	0.86	.45	2.04	.00*

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05*

3.6. Memory Function - Extended Trials

3.6.1. Exploratory Data Analysis

A summary of participants' raw scores for the extended (referring to one-week delay) memory trials is provided in Table 14. Taken together, results of Shapiro-Wilk's test and plotted data suggest assumptions of normality are upheld for the majority variables, with the exception of TLE participants' performance on VPA recall and control participants' performance on VR recognition (see Appendix 19 for histograms).

Table 14

Descriptive Statistics for Extended Memory Trials

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WMS LM Extended Recall	**TLE**	14.16	7.29	4	29	0.61	-0.31	.08
	Control	21.62	5.75	8	34	-0.05	0.34	.96
WMS LM Extended Recog.	**TLE**	21.56	4.19	16	29	0.26	-1.42	.02
	Control	23.85	2.69	19	29	0.19	-0.31	.53
WMS VPA Extended Recall	**TLE***	4.64	2.48	1	11	1.14	0.93	.01
	Control	7.88	2.93	3	13	0.12	-0.84	.39
WMS VPA Extended Recog.	**TLE**	33.88	4.59	21	40	-0.96	1.26	.12
	Control	37.23	2.44	32	40	-0.49	-0.80	.03
WMS VR Extended Recall**	**TLE**	14.13	8.40	0	37	0.84	1.28	.26
	Control	27.27	9.88	9	43	-0.07	-0.93	.38
WMS VR Extended Recog.**	**TLE**	5.00	1.59	2	7	-0.64	-0.47	.02
	Control*	6.08	1.20	2	7	-1.82	4.25	.00

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *non-normal distribution; **data based on 24/25 TLE participants*

3.6.2. Group Comparisons

Levene's test suggests homogeneity of variance is violated for all distributions except LM recognition. From the means (Table 14), it appears that control participants scored higher on all extended memory trials. In line with this, Eta suggests a large between-group difference for recall and a medium-sized difference for recognition on all tasks. This was statistically significant for all variables except LM recognition. See Table 15.

Table 15

Between-Group Comparisons for Extended Memory Trials

	Homogeneity of Variance		**ANOVA**		**Brown-Forsythe**		**Measures of Association**	
	F	**Sig.**	**F**	**Sig.**	**Stat.**	**Sig.**	**η**	**η^2**
WMS LM Extended Recall	2.73	.02*			45.62	.00*	.50**	.25
WMS LM Extended Recog.	0.93	.54	0.93	.57			.32**	.10
WMS VPA Extended Recall	2.62	.02*			48.24	.00*	.52**	.27
WMS VPA Extended Recog.	4.96	.00*			36.25	.00*	.42**	.18
WMS VR Extended Recall* **	5.75	.00*			47.69	.00*	.59**	.35
WMS VR Extended Recog.* **	7.72	.00*			42.67	.01*	.37**	.13

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05; **η>.3; ***data based on 24/25 TLE participants*

3.7. Multivariate Analysis

3.7.1. Covariate Selection

Spearman's Rho correlations were run on all non-memory variables, where significant between-group differences were found. Significant positive correlations were found between PSQI, HADS Anxiety and HADS Depression scores. Significant positive correlations were also found between Visual Puzzles and Category Fluency, as well as all three verbal fluency tasks (Category Fluency, Switch Total, Switch Accuracy). It was therefore decided to consider the contribution of participants' HADS Total (combined anxiety and depression raw scores), Visual Puzzles and Switch Total scores within the multivariate GLM analysis to minimise co-linearity of variables. See Tables 16 and 17.

Table 16

Spearman's Rho Correlation Coefficients for the PSQI and HADS

	PSQI	**HADS Anxiety**
HADS Anxiety	.45*	
HADS Depression	.46*	.61*

**p<.01*

Table 17

Spearman's Rho Correlation Coefficients for Non-Memory Cognitive Variables

	WAIS Visual Puzzles	**DKEFS Category Fluency**	**DKEFS Switch Total**
DKEFS Category Fluency	.37*		
DKEFS Switch Total	.25	.61*	
DKEFS Switch Accuracy	.22	.54*	.95*

**p<.01*

3.7.2. Memory Recall - Standard (30-minute) Delay

Taken together, results of Shapiro-Wilk's test and the data plots suggest residual normality for all three of the 30-minute delayed recall memory variables (see Table 18). Levene's test suggests the assumption of equality of error variances is also upheld for LM, $F(1,49)=2.89$, p=.10, VPA, $F(1,49)=0.63$, p=.43, and VR, $F(1,49)=0.19$, p=.67.

Table 18

Descriptive Statistics for Delayed Recall Memory Residuals

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WMS LM Delayed Recall	**TLE**	0.00	3.38	-6.17	6.19	-0.03	-0.72	.85
	Control	0.00	2.44	-5.61	3.41	-0.68	0.07	.16
WMS VPA Delayed Recall	**TLE**	0.00	2.77	-7.03	5.32	-0.60	0.91	.30
	Control	0.00	2.26	-6.04	3.28	-0.90	0.79	.15
WMS VR Delayed Recall	**TLE**	0.00	2.47	-4.53	7.30	0.77	2.00	.28
	Control	0.00	2.38	-3.37	4.34	0.29	-0.98	.19

LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction

Multivariate GLM suggests that when HADS Total Score, Visual Puzzle and Switch Total performance are also taken into account, group only makes a significant unique contribution to participants' scores on VPA (delayed recall). In comparison, group does not make a significant unique contribution to participants' delayed recall performance on either LM or VR. Performance on Visual Puzzles is suggested to make a significant unique contribution to participants' delayed recall on the VR task and predicts 12% of the variance. See Table 19.

Table 19

Multivariate Analysis of Delayed Recall Tasks

Contributor	Criterion	F	Sig.	η	η^2
Group	**WMS LM Delayed Recall**	0.07	.79	.04	.00
	WMS VPA Delayed Recall	9.50	.00*	.41**	.17
	WMS VR Delayed Recall	2.19	.15	.21	.05
HADS Total Score	**WMS LM Delayed Recall**	0.65	.43	.12	.01
	WMS VPA Delayed Recall	0.05	.83	.03	.00
	WMS VR Delayed Recall	3.50	.07	.27	.07
WAIS Visual Puzzles	**WMS LM Delayed Recall**	2.42	.13	.22	.05
	WMS VPA Delayed Recall	0.66	.42	.12	.01
	WMS VR Delayed Recall	6.16	.02*	.34**	.12
DKEFS Switch Total	**WMS LM Delayed Recall**	3.65	.06	.27	.07
	WMS VPA Delayed Recall	0.04	.84	.03	.00
	WMS VR Delayed Recall	1.01	.32	.14	.02

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05; **η>.3*

3.7.3. Memory Recall - Extended Delay

Taken together, results of Shapiro-Wilk's test and the data plots suggest residual normality for all three extended recall variables (see Table 20). Levene's test suggests the assumption of equality of error variances is also upheld for LM, $F(1,48)=1.08$, p=.30, VPA, $F(1,48)=1.80$, p=.19, and VR, $F(1,48)=1.37$, p=.25.

Table 20

Descriptive Statistics for Extended Recall Memory Residuals

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WMS LM Extended Recall	**TLE**	0.00	6.72	-10.58	13.59	0.50	-0.40	.38
	Control	0.00	5.63	-11.36	12.34	0.22	0.67	.52
WMS VPA Extended Recall	**TLE**	0.00	2.43	-3.41	5.95	0.91	0.37	.09
	Control	0.00	2.90	-4.79	5.02	0.06	-0.91	.51
WMS VR Extended Recall	**TLE**	0.00	7.75	-14.27	23.36	0.92	2.50	.17
	Control	0.00	8.66	-15.13	14.75	0.12	-0.98	.33

LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction

Multivariate GLM analysis suggests group makes a significant unique contribution (of medium effect size) to participants' performance on each of the extended delay recall tasks, when HADS Total Score, Visual Puzzles and Switch Total are also taken into account. Visual Puzzles is also suggested to make a significant unique contribution to VR extended recall and predicts 15% of the variance. See Table 21.

Table 21

Multivariate Analysis of Extended Recall Tasks

Contributor	Criterion	F	Sig.	η	η^2
Group	**WMS LM Extended Recall**	4.98	0.03	.32**	.10
	WMS VPA Extended Recall	5.40	0.03	.33**	.11
	WMS VR Extended Recall	8.46	0.01	.40**	.16
HADS Total Score	**WMS LM Extended Recall**	0.25	0.62	.07	.01
	WMS VPA Extended Recall	1.49	0.23	.18	.03
	WMS VR Extended Recall	0.58	0.45	.11	.01
WAIS Visual Puzzles	**WMS LM Extended Recall**	2.88	0.10	.24	.06
	WMS VPA Extended Recall	0.00	0.96	.00	.00
	WMS VR Extended Recall	8.01	0.01	.39**	.15
DKEFS Switch Total	**WMS LM Extended Recall**	0.07	0.79	.04	.00
	WMS VPA Extended Recall	0.10	0.75	.04	.00
	WMS VR Extended Recall	0.34	0.56	.08	.01

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05; **η>.3*

3.7.4. Memory Recognition - Extended Delay

Taken together, results of Shapiro-Wilk's test and the data plots suggest normality for the majority of residuals. This is with the exception of the control group's VR distribution, which has positive skew and high kurtosis from a large number of high scoring participants (see Table 22). Levene's test suggests the assumption of equality of error variances is upheld for VPA, $F(1,48)=4.12$, p=.05, and VR, $F(1,48)=2.89$, p=.10, but violated for LM, $F(1,48)=5.96$, p=.02. These findings are interpreted with caution.

Table 22

Descriptive Statistics for Extended Recognition Memory Residuals

		Mean	SD	Min.	Max.	Skew.	Kurt.	Shapiro-Wilk (p)
WMS LM Extended Recog.	**TLE**	0.00	3.51	-6.47	5.02	-0.08	-1.24	0.16
	Control	0.00	2.52	-4.06	5.19	0.60	-0.47	0.18
WMS VPA Extended Recog.	**TLE**	0.00	4.37	-11.47	5.95	-0.99	0.83	0.07
	Control	0.00	2.54	-5.06	4.18	-0.39	-0.49	0.42
WMS VR Extended Recog.	**TLE**	0.00	1.41	-2.47	2.22	-0.21	-0.88	0.15
	Control	0.00	1.13	-3.63	1.98	-1.04	3.41	0.05

LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction

Multivariate GLM suggests group does not makes a significant unique contribution to differences in memory recognition performance at the extended delay, when variables of HADS Total Score, Visual Puzzle and Switch Total performance are also considered. In contrast, visuospatial function is suggested to make a significant unique contribution (of medium effect size) to tasks of LM and VR; performance on the Visual Puzzles task accounts for 16% and 15% of LM and VR performance variance respectively. See Table 23.

Table 23

Multivariate Analysis of Extended Recognition Tasks

Contributor	Criterion	F	Sig.	η	η^2
Group	**WMS LM Extended Recog.**	2.01	.16	.21	.04
	WMS VPA Extended Recog.	1.77	.19	.19	.04
	WMS VR Extended Recog.	1.83	.18	.20	.04
HADS Total Score	**WMS LM Extended Recog.**	0.87	.36	.14	.02
	WMS VPA Extended Recog.	0.71	.40	.13	.02
	WMS VR Extended Recog.	0.00	.99	.00	.00
WAIS Visual Puzzles	**WMS LM Extended Recog.**	8.24	.01*	.39**	.16
	WMS VPA Extended Recog.	0.95	.34	.14	.02
	WMS VR Extended Recog.	7.94	.01*	.39**	.15
DKEFS Switch Total	**WMS LM Extended Recog.**	2.99	.09	.25	.06
	WMS VPA Extended Recog.	0.98	.33	.14	.02
	WMS VR Extended Recog.	0.31	.58	.08	.01

*LM=Logical Memory; VPA=Verbal Paired Associates; VR=Visual Reproduction; *p<.05; **η>.3*

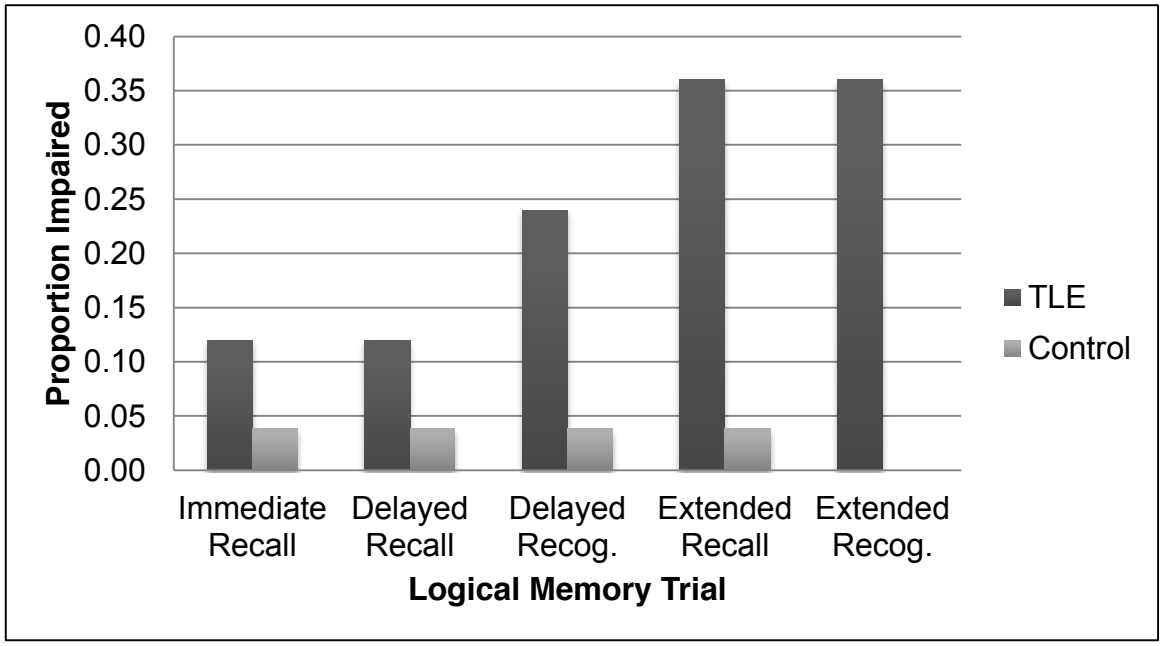
3.8. Individual-Level Analysis

3.8.1. Logical Memory

The proportion of TLE and control participants who had an impaired score (defined as ≤2.0 SDs from the control mean) for each of the LM trials (immediate recall; delayed recall; delayed recognition; extended recall; extended recognition) is shown in Figure 6.

Figure 6

Proportion of TLE and Control Participants with an Impaired Logical Memory Score by Trial



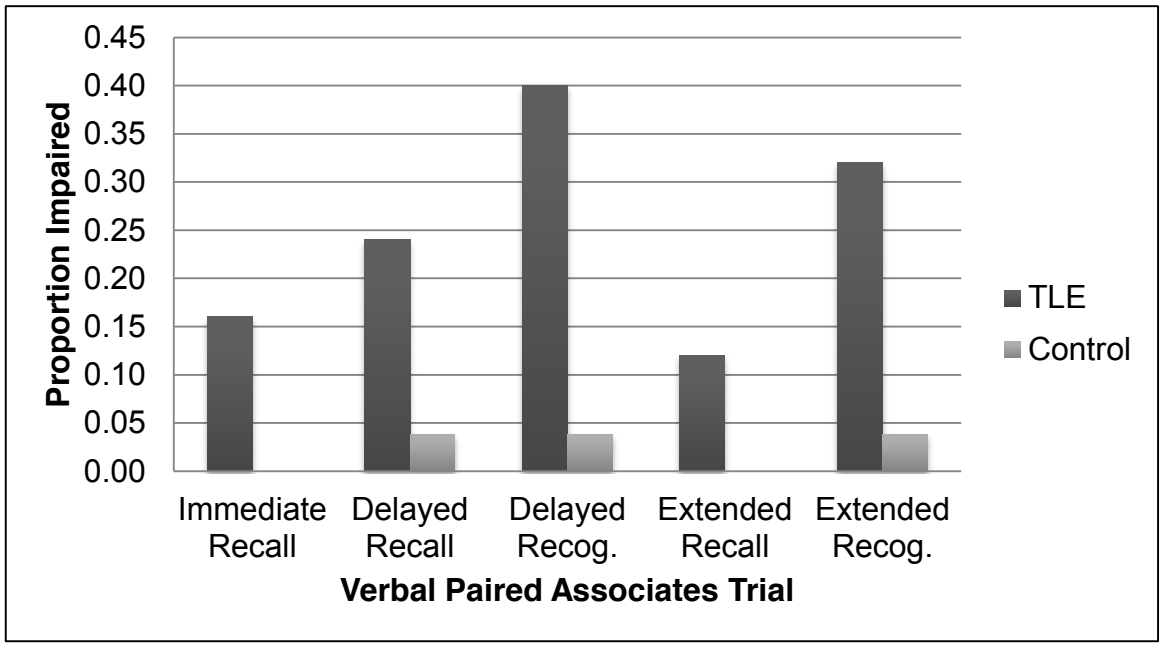
Five TLE participants showed impaired performance on LM recall solely at the extended delay. In comparison, there were no control participants who displayed this pattern of impairment. Additionally, four TLE participants showed impaired performance on LM recognition solely at the extended delay. This was again compared to no control participants.

3.8.2. Verbal Paired Associates

The proportion of TLE and control participants who had an impaired score for each of the VPA trials (immediate recall; delayed recall; delayed recognition; extended recall; extended recognition) is shown in Figure 7.

Figure 7

Proportion of TLE and Control Participants with an Impaired Verbal Paired Associates Score by Trial



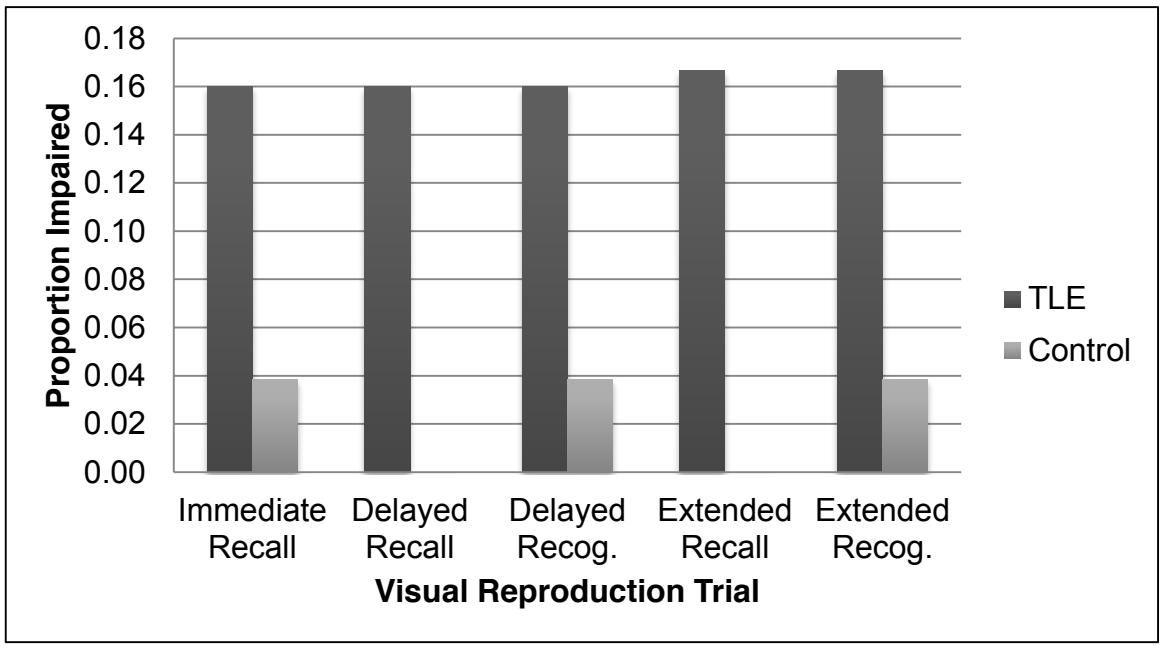
There were two TLE participants who showed impaired performance for VPA recall solely at the extended delay. No control participants showed this pattern of performance. Furthermore, four TLE participants showed impaired recognition performance solely at the extended delay, which was again compared to no control participants.

3.8.3. Visual Reproduction

The proportion of TLE and control participants who had an impaired score for each of the Visual Reproduction trials (immediate recall; delayed recall; delayed recognition; extended recall; extended recognition) is shown in Figure 8.

Figure 8

Proportion *of TLE and Control Participants with an Impaired Visual Reproduction Score by Trial*



There were two TLE participants who showed impaired performance for VR recall solely at the extended delay, where no control participants showed this profile. Similarly, two TLE participants showed impaired recognition performance solely at the extended delay. This was compared to one control participant who displayed this pattern of performance.

3.8.4. Confounding Variables

There were a total of 9 TLE participants and 1 control who displayed impaired memory performance solely at the extended testing delay. Within this sample, 5 of the TLE participants also produced impaired scores on potentially mediating cognitive and non-cognitive variables (cognitive variables ≤2 SDs control mean; non-cognitive variables ≥2 SDs control mean). The remaining 4 TLE participants and 1 control did not produce impaired scores on any of the other assessed cognitive or non-cognitive variables. See Table 24 for further details.

Table 24

Summary of Impaired Performance on Memory, Non-Memory Cognitive and Non-Cognitive Variables

No.	Group	Impaired Memory Performance	Impaired Cognitive Performance	Impaired Non-Cognitive Performance
4	TLE	LME Recall	X	X
6	TLE	VRE Recall	X	X
12	TLE	LME Recog.	X	PSQI HADS Anxiety HADS Depression
14	TLE	LME Recall LME Recog.	X	X
15	TLE	VPAE Recog.	DKEFS Category Fluency DKEFS Switch Total	HADS Depression
17	TLE	LME Recall LME Recog. VPAE Recall VPAE Recog. VRE Recall VRE Recog.	X	X
18	TLE	VPAE Recog. VRE Recog.	DKEFS Category Fluency DKEFS Switch Total	X
19	TLE	LME Recall LME Recog. VPAE Recall VPAE Recog.	X	PSQI HADS Depression
24	TLE	LME Recall	DKEFS Switch Total	HADS Anxiety
43	Control	VRE Recog.	X	X

LME=Logical Memory Extended; VPAE=Verbal Paired Associates Extended; VRE=Visual Reproduction Extended

4. DISCUSSION

This section of the thesis will initially provide a summary of findings; the reader will be re-oriented to the research aims followed by an examination of results in relation to the research questions, the wider literature and original research project (Crowley, 2014). The next sub-section comprises a critical review. Following this, conclusions, clinical implications and directions for future research are given.

In an attempt to support reader clarity, the following WMS-IV^{UK} subtest abbreviations are re-visited:

- VPA = Verbal Paired Associates (word-pair task; verbal [material-specific])
- LM = Logical Memory (story task; verbal [semantic-episodic])
- VR = Visual Reproduction (figure task; visual)

4.1. Summary of Findings

4.1.1. Revisiting the Research Aims

The present study aimed to assess the utility of WMS-IV^{UK} subtests (VPA, LM, VR), when adapted to include an additional one-week testing delay, at detecting ALF in TLE.

The following issues were identified within the literature review and addressed:

- The existing research uses a variety of different assessment tools delivered over a range of testing delays to assess ALF in TLE. As a result findings are varied and interpretations made across research are limited. This was addressed by adapting subtests from an existing and widely used neuropsychological measure (WMS-IV^{UK}; Wechsler, 2010b), to include an

additional one-week testing delay, in an attempt to assess its utility at assessing ALF in TLE.

- The existing research has largely failed to assess the other cognitive domains (attention, verbal, visuospatial and executive function), rendering it unable to account for their potential influence on memory performance. This was addressed by administering a comprehensive neuropsychological test battery, alongside measures of memory, so that potentially mediating cognitive variables could be assessed.

- The existing group-level research has largely failed to provide individual-level analysis, which has resulted in limited knowledge about the proportion of TLE individuals affected by ALF in each sample, the probable inclusion of affected and unaffected individuals, and the likely dilution of any observed between-group differences attributable to ALF. This was addressed by providing both group- and individual-level analysis.

4.1.2. Overview of Demographic Variables

Results suggest the TLE and control group were well matched in terms of age, gender, education and estimated premorbid ability. Accordingly, differences in these variables are unlikely to have influenced memory or cognitive task performance.

Differences were seen on measures of sleep quality, anxiety, depression and self-reported memory, where TLE participants scored significantly higher (with higher scores denoting a higher level of difficulty) than controls. This is well documented within the literature. Research suggests individuals with epilepsy are more likely to experience symptoms of depression and anxiety (Baker et al., 2005) due to negative physical (Fisher et al., 2000) and social (Morrell, 2002) consequences of the illness. Furthermore, specific ALF research has consistently found TLE participants score higher on the HADS than controls (Butler et al., 2009; Mameniskiene et al., 2006). In terms of sleep, there is a wide

evidence-base suggesting a positive relationship between sleep disturbance and TLE, with seizure activity and AEDs both put forward as contributing factors (Wiebe, Blume, Girvin, & Eliasziw, 2001). TLE participants have also been shown to score higher on subjective measures of memory difficulty, regardless of performance on standard memory measures (Butler & Zeman, 2008).

Symptoms of depression, anxiety and poor sleep quality have all been related to memory impairment (Dalgleish & Watts, 1990; Walker & Stickgold, 2006). Although the subjective nature of scores derived from each of these self-report measures is acknowledged, between-group differences are considered within the analysis (see Section 4.1.5.).

4.1.3. Research Question 1

What is the utility of WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction), when adapted to include a one-week testing delay, at detecting ALF in ***a group*** of individuals with TLE compared to a group of unaffected controls?

4.1.4. Interpretation of Findings

4.1.4.1. Standard Testing Delays

The TLE group performed worse than controls on VPA across all three standard trials. They also scored lower than controls on LM and VR delayed recall, and the contribution of participant group to differences in VR delayed recognition was approaching a medium effect. Taken together, results suggest the TLE group experienced difficulty on standard tasks of verbal and visual memory when compared to the current control group. In line with existing research, findings suggest memory difficulties in individuals with TLE can be detected by standard measures of verbal (Butler et al., 2012; Lucchelli & Spinnler, 1998) and visual (Bell et al., 2005; Bengner et al., 2006) memory and challenge suggestions of standard neuropsychological tools as inadequate at detecting memory impairment in TLE (Fitzgerald, Mohamed, et al., 2013).

A distinction between verbal material-specific and verbal semantic-episodic memory is suggested by the differences observed in the TLE groups' performance on VPA and LM. The TLE group performed worse than controls on LM delayed recall, despite apparently matched performance at immediate recall and delayed recognition, which suggests difficulty in verbal semantic-episodic retrieval. In contrast, lower scores across all three standard trials of VPA appear to suggest difficulty in verbal material-specific learning. In terms of visual memory, TLE participants performed worse than controls on VR delayed recall and recognition but not immediate recall, which may suggest difficulty in visual memory consolidation. Findings are consistent with a distinction between processes of learning and memory as well as systems of verbal, visual, semantic-episodic and material-specific information (Matlin, 2005).

4.1.4.2. Extended Testing Delays

The TLE group also performed worse than controls at the extended (one-week) testing delay on tasks of recall and recognition for all three adapted WMS-IV^{UK} subtests. Participant group made a medium-size contribution to recognition performance and a large-size contribution to recall. Between-group differences were statistically significant across all extended subtests with the exception of LM recognition (it is likely this was a consequence of small sample size; Brown, 2008).

In line with much of the existing literature, findings suggest TLE participants perform worse than controls when memory is assessed at extended delays and that this is more prominent on tasks of recall than recognition (Butler et al., 2013; Jansari et al., 2010; Kapur et al., 1997). The differences observed between groups at the standard testing delays (with TLE participants performing worse than controls) make it difficult to ascertain whether the TLE group displayed an additionally accelerated rate of forgetting, or whether the differences in memory performance at the extended delay were solely attributable to initial differences in encoding and/or retrieval.

4.1.4.3. Normative Comparisons

In order to ascertain the generalisability of control group comparisons, the performance of both groups was compared with WMS-IV^{UK} population norms for each of the standard memory trials. The control group performed higher than expected on all but one (VPA immediate recall) of the recall trials. In contrast, the TLE group only performed lower on VPA. Thus, in relation to a normative population, results do not suggest evidence of TLE group impairment on either LM or VR. With this in mind, the differences observed between TLE and control groups on LM and VR at the extended delay may simply reflect an exacerbated effect caused by the control groups' above average performance. Alternatively, large increases in effect size between 30-minute's (standard) and one-week's (extended) delay (with the variance in scores attributable to participant group increasing by over 50% for LM and 30% for VR; see Tables 12 and 15) may suggest evidence of an additionally accelerated rate of forgetting in the TLE group for both measures. Despite this, the presence of a group memory profile consistent with current definitions of ALF (Butler & Zeman, 2008) remains impossible to ascertain, as between-group memory performance was not comparable at standard delays.

4.1.4.4. Summary

Results suggest the TLE group performed worse than controls on VPA, LM and VR at both standard and extended testing delays. Taken at face value, findings suggest TLE group primary difficulty in the initial encoding/retrieval of novel information (rather than ALF). However, the interpretation is confounded by the above average performance of control participants on all standard memory measures. This complicates understanding of whether between-group differences at the extended delay on LM and VR (where the TLE group performed in line with normal data) were relative to the control group's superior performance, versus additionally influenced by an accelerated rate of forgetting. Increases in effect size (from delayed to extended trials) appear to support the latter interpretation, which would suggest the utility of WMS-IV^{UK} subtests LM and VR at detecting verbal and visual ALF. However, this cannot be ascertained due to the presence of between-group memory performance differences when assessed at standard delays.

4.1.5. Research Question 2

What is the influence of non-memory cognitive performance on the presentation and detection of ALF in ***a group*** of individuals with TLE (compared to unaffected controls) when assessed using WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction) with an additional one-week testing delay?

4.1.6. Interpretation of Findings

4.1.6.1. Performance on Non-Memory Cognitive Domains

Differences were found between the TLE group and test-manual norms on tasks of processing speed; and TLE participants performed significantly worse than expected. Processing speed difficulties are well documented in TLE (Dow, Seidenberg, & Hermann, 2004), and have been associated with generalisation of seizure activity (Tromp et al., 2003) and the negative side effects of AEDs (Hessen, Lossius, Reinvang, & Gjerstad, 2006). Control participants also performed slightly lower than average on the processing speed task. As a result no significant between-group differences were found.

In terms of visuospatial function, control participants performed significantly better than the normative sample. This is likely to have contributed to the between-group differences observed on this task, where TLE participants performed worse than controls. Difficulties on tasks of visuospatial function are not uncommon in TLE and often result from seizure activity in the right TL (Blaxton & Theodore, 1997).

Finally, the TLE group also performed significantly lower than test-manual norms on a task of verbal executive functioning (Switch Total). Findings are in line with research suggesting the role of the TLs (specifically left hemisphere) in verbal fluency (Tröster et al., 1995), and relationship between TLE and difficulty on tasks of executive function (Keller et al., 2009). In contrast, the control group performed significantly higher than average on all four executive tasks. As a result, between-group differences are seen in verbal executive function.

No differences were observed between-groups, or in relation to the normative sample, on tasks of attention (short-term and/or working memory) or general verbal function.

4.1.6.2. The Impact of Non-Memory Functions on Memory Performance

The areas of cognitive function where between-group differences were seen have been suggested to mediate memory performance; verbal fluency is related to verbal semantic memory (Duff et al., 2005) and visuospatial function underpins visual memory (Park et al., 2002). With this in mind, further multivariate analysis was conducted to assess the influence of these variables on memory performance.

Between-group differences in non-cognitive functioning (as assessed on the HADS and PSQI) were also considered, as poor sleep and symptoms of anxiety and depression have also been linked with memory impairment (Dalgleish & Watts, 1990; Walker & Stickgold, 2006). Due to co-linearity between measures of verbal fluency and visuospatial function, and mood and sleep (see Tables 16 and 17), scores for only the following measures were included as covariates; DKEFS Switch Total, WAIS Visual Puzzles and HADS Total Score.

When measures of mood, visuospatial function and verbal fluency were considered together with participant group, a different pattern of results emerged. In terms of delayed (standard 30-minute) recall, group membership no longer predicted memory performance for either LM or VR. Instead, performance on the visuospatial task contributed to VR scores. In comparison, group did make a unique contribution to VPA delayed recall, and TLE participants were still observed to perform significantly worse than controls.

In contrast, at the extended (one-week) delay, group made a significant unique contribution to memory recall on all three measures and the TLE group performed worse than controls. Additionally, the relationship between visuospatial performance and VR remained. However, in terms of recognition memory (also at the extended delay), group was not observed to contribute to participants' performance on any of the memory measures. Instead, poor

visuospatial performance contributed to difficulty on VR, and unexpectedly also contributed to difficulty on LM. A correlation between Visual Puzzles and one of the verbal fluency tasks (DKEFS Category Fluency) may somewhat explain this unusual finding, with visual memory difficulty more commonly linked to general visual function (Duff et al., 2005).

Taken together, when measures of mood, visuospatial function and verbal fluency are considered, an accelerated rate of forgetting (previously obscured by between-group differences on the non-memory variables) can be observed in the TLE group for LM and VR: TLE participants' recall performance was significantly worse than controls on these measures at the one-week delay, despite being comparable at the standard delay. This profile appears consistent with current definitions of ALF (Butler & Zeman, 2008). In comparison, the presence of an accelerated rate of forgetting, consistent with current definitions of ALF, cannot be ascertained for VPA due to the differences observed between groups at the standard delay. The control group's above average performance on this subtest remains an issue for interpretation.

Results are in line with research that has interpreted the presence of ALF for visual figure reproduction (Cronel-Ohayon et al., 2006; Gallassi et al., 2011) and verbal story recall (Manes et al., 2005; Manning et al., 2006) following extended delays. Findings also align with Bell (2005), who demonstrated impaired TLE group performance for verbal material-specific information (word list recall) at 30-minutes that persisted across extended delays, as well as studies reporting a higher frequency of material-specific memory difficulties in people with TLE (Dupont et al., 2000). Differences in the TLE group's performance on VPA and LM may provide further support for a distinction between ALF for verbal semantic-episodic and material-specific information (Gallassi et al., 2011). Furthermore, in line with previous research (Hoefeijzers et al., 2013; Kemp et al., 2012), differences in the TLE group's performance on tasks of extended recall and recognition suggest a distinction between ALF for these processes. Contradictory to research demonstrating a similar pattern of ALF for both recall and recognition (Jansari et al., 2010; Manes et al., 2005; Mayes et al., 2003), the present TLE group appear to display exacerbated difficulty in the extended free

recall of novel information as opposed to a rapid decay, which would have been apparent also on recognition formats. It is possible that at longer testing delays, an accelerated rate of forgetting for the recognition task may have also been observed (Hoefeijzers et al., 2013).

4.1.6.3. Summary

Results suggest the utility of WMS-IV^{UK} subtests LM and VR at detecting verbal and visual ALF in a group of individuals with TLE, when the contribution of between-group differences in visuospatial function, verbal fluency and mood are considered. In doing so, findings demonstrate the mediating role of non-memory cognitive and non-cognitive variables on the presentation and detection of ALF in a group of individuals with TLE. These results emphasise the importance of attending to between-group differences in non-memory variables, which when left unaccounted for may obscure accelerated forgetting at a group level. The mediating role of visuospatial function in memory performance, as well as the role of mood, verbal fluency and visuospatial function when combined, is reiterated.

The present research was unable to ascertain the utility of VPA at detecting ALF in a group of individuals with TLE, even when non-memory variables were considered, due to between-group differences in memory performance at the standard testing delay.

It is important to acknowledge that the present pattern of between-group difference (with TLE impairment at the standard delay for VPA and extended delay for LM and VR) is likely to reflect a combined memory profile for the present TLE group as opposed to this population more generally. Furthermore, findings are in relation to the present control group; the generalisability of this sample to a wider population is limited.

4.1.7. Research Question 3

What is the utility of WMS-IV^{UK} subtests (Verbal Paired Associates, Logical Memory, Visual Reproduction), when adapted to include a one-week testing delay, at detecting ALF in ***individuals***?

4.1.8. Interpretation of Findings

Results of the individual analysis identified nine TLE participants who displayed impaired memory performance (when compared to the control group) on one or more of the three WMS-IV^{UK} subtests (VPA, LM, VR) for tasks of both extended recall and recognition. This was despite apparently normal performance when tested using WMS-IV^{UK} standard delay procedures. These findings suggest an accelerated rate of forgetting for new information in over a third of the present TLE group, whose profiles appear consistent with current definitions of ALF (Butler & Zeman, 2008).

A varying pattern of memory difficulty was recorded across these nine TLE participants (see Table 24). Evidence of accelerated forgetting for only one of the three subtests (LM, VPA, VR) was displayed in some individuals. In comparison, other individuals displayed accelerated forgetting for two or all three of the subtests. Furthermore, evidence of individuals displaying accelerated forgetting for recall but not recognition as well as both recall and recognition was also observed. Additionally, three of these TLE participants displayed impaired performance solely for the extended recognition element of a task despite apparently intact free recall. Taken together, results suggest a diverse nature to ALF as it occurs across the different memory modalities (e.g. verbal semantic-episodic, verbal material-specific, visual) and processes (e.g. recall versus recognition), which produces a unique pattern of impairment in individuals. This may provide some explanation for the variation in findings across current research (Bell, 2006; Butler et al., 2007; Gallassi et al., 2011; Jansari et al., 2010).

It must be acknowledged that five of the nine TLE participants who displayed an accelerated rate of forgetting within the individual analysis also displayed impaired performance (in relation to current controls) on measures of semantic fluency, sleep quality, depression and anxiety (see Table 24). Furthermore, the three TLE participants who displayed the unusual profile of ALF for tasks of recognition, despite apparently intact free recall, also fell within this sub-group. As already discussed, the non-memory variables listed above have all been

shown to affect memory performance (Dalgleish & Watts, 1990; Duff et al., 2005; Walker & Stickgold, 2006). Although it is beyond the scope of this thesis to investigate further, it is important to consider that the memory profiles observed in this sub-group of individuals may have been mediated by cognitive and/or non-cognitive variables.

Interestingly, there was one control participant who performed within the impaired range for VR extended recognition, despite apparently normal performance on all other variables. The presence of ALF in normally developed / neurologically intact individuals is an area yet to be investigated. These findings may suggest accelerated forgetting is not specific to TLE but a wider memory deficit that clinicians should be aware of. On the other hand, this participant's extended memory profile (with impaired performance solely for the recognition element of VR despite normal extended recall) may be more sensible to interpret as an attentional lapse (Robinson, 1995). Further assessment of this participant would be necessary before any valid hypotheses could be drawn.

4.1.8.1. Summary

Results of the individual analysis suggest evidence of accelerated forgetting in over one third of the TLE participants, whose memory profiles were consistent with current definitions of ALF (Butler & Zeman, 2008). Accelerated forgetting was observed on all three of the investigated WMS-IV^{UK} subtests (LM, VPA, VR), and for tasks of both recall and recognition. Variation in extended memory performance between these participants suggests the unique nature of accelerated forgetting, which appears to produce an individualised pattern of impairment in those affected. The utility of WMS-IV^{UK} subtests VPA, LM and VR at detecting ALF in individuals with TLE is supported.

The role of impaired performance on potentially mediating cognitive and non-cognitive variables, occurring in over half of the TLE individuals whose memory profiles aligned with current definitions of ALF, needs further investigation before more confident interpretations of the phenomenon can be made. Furthermore, interpretation is limited by above-average control group performance, when compared to test-manual norms.

4.1.9. Revisiting the Initial Study

The present study aimed to build upon the findings of a previous doctoral research project (Crowley, 2014) in the following ways:

- Recruiting additional TLE and control participants to create a larger and more representative sample.

- Providing additional individual-level analysis, alongside group-level analysis, with the larger sample.

- Providing additional multivariate analysis to assess the influence of between-group differences on non-memory variables.

4.1.9.1. Summary of Findings

The original study recruited a sample of 14 TLE and 16 control participants. Reliable differences (with TLE participants performing worse than controls) were seen between groups on standard trials of VPA, VR and LM. However, in relation to the WMS-IV^{UK}'s normative sample, TLE group differences were only seen for VPA. Problematically, the control group performed better than expected on LM, VR and VPA.

At the extended delay, the TLE group also performed significantly worse than controls on LM, VR and VPA. Effect sizes were not calculated. In terms of non-memory cognitive variables, TLE participants performed significantly worse than controls on measures of verbal fluency, processing speed and visual attention span.

It was concluded that when assessed at standard delays, the WMS-IV^{UK} was sensitive to subtle TLE group memory impairments, which may have gone undetected by less modern batteries. These memory difficulties became more pronounced at the extended delay but were not consistent with current descriptions of ALF. Recommendations were made for further analysis with a

larger sample and additional assessment of the role of cognitive contributory factors.

4.1.9.2. Evaluation of Present Research in Relation to the Initial Study

The present research added an additional 11 TLE and 10 control participants, who were recruited from a wider geographical location, with the additional inclusion of Epilepsy Action (EA) as a novel recruitment site. Strategic sampling attempted to further align the control group with normative data, however analysis suggested that this group still performed better than expected on all three WMS-IV^{UK} memory subtests.

As with the previous study, between-group differences were found on VPA, LM and VR at both standard and extended testing delays. However, the additional inclusion of multivariate analysis that considered the influence of non-memory cognitive and non-cognitive variables (where initial between-group differences were demonstrated) yielded a different pattern of results; and evidence of accelerated forgetting was observed across the TLE group on measures of LM and VR. Interpretation of accelerated forgetting for VPA remained unclear due to differences in performance between groups at the standard delay. The inclusion of individual-level analysis provided additional information about the proportion of TLE individuals that displayed an accelerated rate of forgetting within the present sample and evidenced a memory profile consistent with current definitions of ALF on all three WMS-IV^{UK} subtests (LM, VPA, VR).

4.2. Critical Evaluation

4.2.1. Strengths

Building upon the research of Crowley (2014), the present study comprised one of the first to investigate the utility of WMS-IV^{UK} subtests (VPA, LM, VR) at assessing ALF in a group of individuals with TLE. Previous research has utilised a variety of out-dated measures to assess this novel construct (Bell, 2006; Kemp et al., 2012; Manes et al., 2005), which has complicated interpretation across

research and the utility of findings for clinical practice. In contrast, the WMS-IV^{UK} is the world's most commonly used memory assessment tool (Drozdick et al., 2011), which strengthens both the clinical validity and utility of findings.

The present study built upon findings by Crowley (2014) by adding additional participants, which enabled the utilisation of more detailed multivariate analysis. Furthermore, the addition of EA as a second recruitment site provided a wider geographical sample of TLE participants and enhanced generalisability to a wider population of individuals with TLE.

To my knowledge, together with the original study by Crowley (2014), this research comprises the first to administer a comprehensive neuropsychological assessment battery (across all cognitive domains of processing, attention, general verbal and visuospatial function, executive function, and memory) to both TLE and control participants. Furthermore, this specific study is the only one within its field to fully assess and consider the influence of between-group differences in cognitive function, as well as suggest the role of mediating cognitive variables upon the presentation and detection of ALF in group-level research. On top of this, non-cognitive variables (e.g. mood, sleep, education and age) were also considered.

The present research is one of only two (Evans, Elliott, Reynders, & Isaac, 2014) to include both group- and individual-level analysis with TLE participants displaying accelerated forgetting. In doing so, this study was able to provide some understanding of the proportion of individuals affected by ALF within the sample, illustrate a variety of ALF profiles across individuals, and provide evidence for the utility of each of the three WMS-IV^{UK} subtests (VPA, LM, VR) at detecting ALF in TLE.

All measures used to assess both memory and non-memory cognitive functions were current, widely used in both research and clinical practice, and evidenced as valid and reliable tools. Alongside between-group comparisons, this enabled each group to also be compared with robust normative data.

Finally, recommendations for conducting research into ALF in TLE, as laid out by Elliott, Isaac and Muhlert (2014), were adhered to. Groups were well matched by age, gender, education and estimated premorbid ability. Visual (VR) and two types of verbal (LM; semantic-episodic, and VPA; material-specific) material were used to assess the different memory modalities on tasks of both recall and recognition. Floor and ceiling effects were avoided by (a) using reliable and valid assessment tools, and (b) setting extended testing delays to exactly one-week; a time-frame that has been shown as reliable in the assessment of ALF in TLE (Butler et al., 2013; Gallassi et al., 2011). Additionally, rehearsal between testing intervals was avoided by (a) administering neuropsychological tests between immediate and delayed (30-minute) recall, and (b) not informing participants that memory would be re-assessed at the extended (one-week) testing delay.

4.2.2. Limitations

Despite the strengths outlined above, any interpretation of the present findings must acknowledge the following limitations. Firstly, interpretation of ALF in the TLE group is complicated by the control group's above-average performance (when compared to WMS-IV^{UK} normative data) on each of the memory subtests (LM, VPA, VR). This makes it difficult to conclude whether the differences observed between TLE and control participants on each of the memory subtests would still have been present if the control group had comprised a more representative sample. The control groups' above average memory performance may reflect a particular and unusual property of this group, who were self-selected and highly motivated. Additionally, despite adhering to WMS-IV^{UK} administration procedures, this pattern of results may also reflect an unidentified difference in test administration. In comparison, the control group's above-average performance could point to an issue with the UK validation study (Wechsler, 2010b). However, this appears less likely when the scale and resource of this study are considered.

Interpretations of ALF are also limited by the use of raw (versus age-scaled) scores to make group comparisons at the extended delay. This was necessary due to the unavailability of age-scaled scores for the WMS-IV^{UK}, when

administered with extended (one-week delay) procedures. However, as a result, interpretation of accelerated forgetting across testing delays (standard to extended) remains at a theoretical level.

Recommendations for research investigating ALF in TLE (Elliott et al., 2014) suggest matching participants by learning; for example learning to a criterion. This was not adhered to in the present design as WMS-IV^{UK} administration procedures were adopted. It is possible that matching groups in this way could have somewhat alleviated concerns about the control group's above-average memory performance and impact of this upon ascertaining the presence of accelerated forgetting within the TLE group. On the other hand, matching participants in this way could itself be criticised for encouraging over-learning in a way that compromises ecological validity. Furthermore, it is likely the groups would require unequal learning opportunities to meet the same criterion (Djordjevic et al., 2011) and little is known about the impact of this upon forgetting (Elliott et al., 2014).

The present research utilised just one extended testing delay (one-week) to assess ALF. Incorporating more regular testing delays (Kemp et al., 2012) could have provided additional information about the onset of ALF as well as any potential differences in onset between TLE participants. However, this would also have resulted in the additional rehearsal of material, which in itself may have somewhat counteracted the investigation of ALF; research suggests repetition can alleviate this memory impairment (McGibbon & Jansari, 2013).

Finally, it is acknowledged that there is a vast research-base suggesting the role of epilepsy characteristics on memory and cognition. These include seizure type (Fitzgerald, Thayer, et al., 2013), duration (Hermann et al., 2002), severity (Berg, 2011), seizure lateralisation (Bengner et al., 2006) and aetiology (Berg, 2011) as well as differences in AED use (Helmstaedter & Kurthen, 2011). Unfortunately, due to both the scope of this project and size of the sample, it was not possible to undertake further analysis into each of these variables, which may have been found to have a mediating effect on the TLE participants' memory performance.

4.2.3. Research Reflexivity

Reflexivity within research refers to consideration of the circular and self-perpetuating relationship between researcher, his/her social context and history, and resulting research (Flanagan, 1981). Reflecting upon my own social context has illustrated its influence upon the questions I asked, methodology I chose and interpretations I developed.

Within the methods, I state my decision to take a critical realist approach. This aligned with my own curious and ever-questioning stance, shaped by my family's demand for nothing to be taken for granted, without question or second-thought, as well as the hugely influential, critical and thought-provoking doctoral training I have embarked upon. In taking this approach I acknowledge the cognitive domains as fluid and social constructs. However, despite this I still make attempts to measure the behavioural output of these socially constructed categories. Growing up in an era where computers and technology are considered normal and even vital to every-day existence has perhaps drawn me to a metaphor of memory as a flow of information, travelling between distinct systems. For me, it seems a logical and sensible way to somehow grapple with these more abstract concepts, whilst still keeping the limitations of the approach in mind. Furthermore, from the context of being a Trainee Clinical Psychologist, neuropsychological assessment seemed an obvious way of attempting to assess and understand constructs of "memory" and "forgetting".

In undertaking this research, my more "critical" self has questioned the methodology; I hold concerns about contributing to a body of research and social discourse that reifies "impairments" in memory and cognitive function as internalised and fixed, as opposed to relational and context-dependent. I also worry my findings will support the marketisation of instruments whose self-perpetuating and circular relationship with diagnosis are often driven by economics rather than the best interests of the individual. However, the "realist" in me balances these concerns with genuine belief in the necessity for 1) this experience ("ALF") to be better understood, (2) clinicians assessing constructs of "learning" and "memory" to consider more novel cognitive profiles, which may

align with definitions of ALF, and (3) people experiencing accelerated forgetting in relation to what is currently considered "normal" not to be discounted by standard neuropsychological measures but provided with the appropriate support and/or intervention.

In writing, I reflect that my chosen methodology comprised just one way of investigating a novel construct ("ALF"). Although it arguably fitted with the dominant approach to this type of research and current scientific paradigm, it was by no means the only possible route. For example, coming at this from a phenomenological perspective may have instead resulted in a qualitative analysis of TLE participants' subjective experience of "forgetting", which would have produced very different findings. The point I attempt to make is that I believe there is no right way of approaching this work, no absolute truth or truly "valid" result to be found but multiple perspectives, approaches and interpretations, resulting from the multiple contexts we exist within. What is vital is that this is held in mind alongside the findings and interpretations I present.

4.3. Conclusions

The present research aimed to investigate the utility of WMS-IV^{UK} subtests at detecting ALF in TLE. Preliminary comparatory analysis suggested the TLE group performed worse than controls on all three memory subtests (at both standard and extended testing delays). Consequentially, the presence of accelerated forgetting could not initially be ascertained. However, when the contribution of participants' performance on tasks of visuospatial function and semantic fluency as well as symptoms of anxiety and depression (where initial between-group differences were observed) was also taken into account, a different pattern of results emerged. Once again, at the extended delay group membership made a unique contribution to participants' recall performance on all three WMS-IV^{UK} subtests (LM, VPA, VR). In comparison, when these non-memory variables were also taken into account at the standard delay, group membership was not shown to contribute to memory recall performance for either LM or VR. This pattern of results (with the TLE group performing worse than

controls at the extended delay despite comparable performance at the standard delay) appears to suggest an accelerated rate of forgetting in the TLE group for tasks of visual (VR) and verbal semantic-episodic (LM) memory recall.

Additional individual-level analysis demonstrated a variety of memory profiles in the TLE group. Some TLE participants experienced primary difficulty in the encoding and/or retrieval of new information, detectable across standard delays. It was unclear whether these participants also experienced an additionally accelerated rate of forgetting. In comparison, accelerated forgetting for new information (on all three WMS-IV^{UK} subtests, and on tasks of both recall and recognition) was observed in over one third of the TLE participants. These participants performed worse than controls at the extended delay despite performance being comparable at the standard delay; this memory profile is consistent with current definitions of ALF. Variation between these participants' extended memory performance suggests the unique nature of accelerated forgetting as it presents across the different memory modalities (verbal versus visual) and processes (recall versus recognition).

The utility of all three WMS-IV^{UK} subtests at detecting ALF in TLE is supported. However, findings are limited by the above-average memory performance of control group participants.

4.4. Clinical Implications

Findings of the present research suggest the utility of all three WMS-IV^{UK} subtests (LM, VPA, VR), when adapted to include a one-week testing delay, at detecting verbal (material-specific and semantic-episodic) and visual ALF in individuals with TLE. In doing so, findings provide further evidence to support the existence of this novel memory profile. These findings challenge currently dominant unitary models of memory consolidation (Squire & Alvarez, 1995), and are instead consistent with a more complex and multi-faceted process in the consolidation of longer-term memory.

Current findings suggest that some form (e.g. verbal versus visual) of accelerated forgetting may present in up to a third of individuals with TLE and emphasise the importance of utilising longer testing delays when clinically assessing memory in this population. Results suggest the inclusion of an additional one-week retrieval (recall and recognition) delay would be adequately sensitive to detect a variety of ALF profiles. It is vital that dominant memory assessment tools, such as the WMS-IV^{UK}, develop standardised norms of memory performance at extended delays to support the clinical assessment of memory in individuals with TLE.

The role of cognitive and non-cognitive variables in mediating the memory performance of individuals with TLE is also emphasised. It is important that this is considered within any clinical assessment of memory in TLE.

Results suggest ALF produces a distinct pattern of impairment in those affected, which may present across different memory modalities (verbal, visual) and processes (recall, recognition). The intimation of ALF that affects tasks of memory recall but not recognition in some individuals with TLE does somewhat question current definitions of this novel construct. This specific memory profile may be more accurately described as an accelerated *decline in recall* as opposed to *forgetting*; as theoretically forgetting suggests the loss/decay of memory (Parkin, 1993), which would also be observed on tasks of recognition. However, it should be considered that any broad description/construction of memory performance will obscure more detailed information about an individuals' memory profile and clinically it may be more helpful to describe than categorise individual patterns of performance.

Further evidence for the validity of the WMS-IV^{UK} as an assessment tool for memory difficulty in individuals with TLE is provided. Results suggest the WMS-IV^{UK} is sensitive to a range of memory difficulties that present in people with TLE, when assessed at both standard and extended testing delays.

4.5. Future Research Directions

The development of standardised norms of memory performance at extended testing delays, for all of the currently dominant memory assessment tools, will be of benefit to future research and clinical practice. The availability of this data will overcome current issues faced when attempting to draw conclusions across studies of accelerated forgetting with distinct control-comparison groups as well as aid the clinical assessment of memory difficulties in people with TLE. The findings of the present study suggest that the WMS-IV (which is currently the most widely used memory assessment tool; Drozdick et al., 2011) would be a sensible starting point.

Our current understanding about the exact point/s of onset and course/s of ALF in TLE remains limited. Further longitudinal research comparing rates of forgetting between cognitively intact individuals and those with TLE displaying evidence of ALF would be useful. This will hopefully support the development of extended memory performance norms, by providing additional information about which testing delay/s are important to utilise in the assessment of memory in individuals with TLE.

The present research demonstrates the variety of memory difficulties that present in individuals with TLE. It is important that future group research within this area includes individual-level analysis as standard to ensure the differences in memory performance between TLE participants are considered. Furthermore, group-level analysis should be examining TLE participants by memory profile (e.g. standard versus extended delay impairments) if meaningful comparisons are to be made. Additionally, it is vital that any future research in this area also comprehensively assesses cognitive and non-cognitive variables in both TLE and control participants and that the contribution of any potentially mediating variables (in memory performance) is considered.

Focusing specifically on the present study, findings could be furthered by conducting additional analysis with the existing TLE group, using a more normative control group. Further multivariate analysis, to consider the role of

TLE participants' epilepsy characteristics (e.g. AEDs, seizure hemispheric lateralisation, frequency, type and duration) on memory performance, would also be of benefit if a large enough sample size could be obtained.

REFERENCES

Ahern, G. L., O'Connor, M., Dalmau, J., Coleman, A., Posner, J., Schomer, D., . . . Mesulam, M. (1994). Paraneoplastic temporal lobe epilepsy with testicular neoplasm and atypical amnesia. *Neurology, 44*(7), 1270-1270.

Aldenkamp, A., & Arends, J. (2004). The relative influence of epileptic EEG discharges, short nonconvulsive seizures, and type of epilepsy on cognitive function. *Epilepsia, 45*(1), 54-63.

Aldenkamp, A., Krom, M. D., & Reijs, R. (2003). Newer antiepileptic drugs and cognitive issues. *Epilepsia, 44*(4), 21-29.

Annegers, J. F., Grabow, J. D., Groover, R. V., Laws, E. R., Elveback, L. R., & Kurland, L. T. (1980). Seizures after head trauma: A population study. *Neurology, 30*(7), 683-683.

APA. (2009). *Publication manual of the American Psychological Association*. Washington: American Psychological Association (APA).

Armstrong, C. L., & Morrow, L. (2010). *Handbook of medical neuropsychology: Applications of cognitive neuroscience*. New York: Springer Science & Business Media.

Armstrong, D. M. (1973). *Belief, truth and knowledge*. Cambridge: CUP Archive.

Atkinson, R. C., & Shiffrin, R. M. (1968). Human memory: A proposed system and its control processes. *Psychology of Learning and Motivation, 2*, 89-195.

Baddeley, A. (2000). The episodic buffer: A new component of working memory? *Trends in Cognitive Sciences, 4*(11), 417-423.

Baddeley, A., & Hitch, G. (1974). Working memory. *Psychology of Learning and Motivation, 8*, 47-89.

Baker, G. A., Austin, N. A., & Downes, J. J. (2003). Validation of the Wechsler Memory Scale-III in a population of people with intractable temporal lobe epilepsy. *Epilepsy Research, 53*(3), 201-206.

Baker, G. A., Spector, S., McGrath, Y., & Soteriou, H. (2005). Impact of epilepsy in adolescence: A UK controlled study. *Epilepsy & Behaviour, 6*(4), 556-562.

Beck, A. T., & Steer, R. A. (1990). *Beck Anxiety Inventory.* San Antonio: The Psychological Corporation.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Beck Depression Inventory-II.* San Antonio: The Psychological Corporation.

Beckung, E., & Uvebrant, P. (1993). Motor and sensory impairments in children with intractable epilepsy. *Epilepsia, 34*(5), 924-929.

Bell, B. D. (2006). WMS-III logical memory performance after a two-week delay in temporal lobe epilepsy and control groups. *Journal of Clinical and Experimental Neuropsychology, 28*(8), 1435-1443.

Bell, B. D., Fine, J., Dow, C., Seidenberg, M., & Hermann, B. P. (2005). Temporal lobe epilepsy and the selective reminding test: The conventional 30-minute delay suffices. *Psychological Assessment, 17*(1), 103.

Bender, R., & Lange, S. (2001). Adjusting for multiple testing - when and how? *Journal of Clinical Epidemiology, 54*(4), 343-349.

Bengner, T., Malina, T., Lindenau, M., Voges, B., Goebell, E., & Stodieck, S. (2006). Face memory in MRI-positive and MRI-negative temporal lobe epilepsy. *Epilepsia, 47*(11), 1904-1914.

Benn, E. K., Hauser, W. A., Shih, T., Leary, L., Bagiella, E., Dayan, P., . . . Hesdorffer, D. C. (2008). Estimating the incidence of first unprovoked seizure and newly diagnosed epilepsy in the low-income urban community of Northern Manhattan, New York City. *Epilepsia, 49*(8), 1431-1439.

Bennett, J., & Fisher, R. A. (1995). *Statistical methods, experimental design, and scientific inference*. Oxford: Oxford University Press.

Benson, N., Hulac, D. M., & Kranzler, J. H. (2010). Independent examination of the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV): What does the WAIS-IV measure? *Psychological Assessment, 22*(1), 121.

Berg, A. T. (2011). Epilepsy, cognition, and behaviour: The clinical picture. *Epilepsia, 52*(1), 7-12.

Berg, A. T., Berkovic, S. F., Brodie, M. J., Buchhalter, J., Cross, J. H., Van Emde Boas, W., . . . Mathern, G. W. (2010). Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia, 51*(4), 676-685.

Blake, R., Wroe, S., Breen, E., & McCarthy, R. A. (2000). Accelerated forgetting in patients with epilepsy: Evidence for an impairment in memory consolidation. *Brain, 123*(3), 472-483.

Blaxton, T. A., & Theodore, W. H. (1997). The role of the temporal lobes in recognizing visuospatial materials: Remembering versus knowing. *Brain and Cognition, 35*(1), 5-25.

Bromfield, E. B., Cavazos, J. E., & Sirven, J. I. (2006). *Basic mechanisms underlying seizures and epilepsy*. Connecticut: American Epilepsy Society.

Brown, J. D. (2008). Effect size and eta squared. *JALT Testing & Evaluation SIG Newsletter, 12*(2), 38-43.

Bruce, V., & Young, A. (1986). Understanding face recognition. *British Journal of Psychology, 77*(3), 305-327.

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton tests*. Bury St. Edmunds: Thames Valley Test Company.

Burnham, W. H. (1903). Retroactive amnesia: Illustrative cases and a tentative explanation. *The American Journal of Psychology*, *14,* 382-396.

Butler, C. R., Bhaduri, A., Acosta-Cabronero, J., Nestor, P., Kapur, N., Graham, K., . . . Zeman, A. (2009). Transient epileptic amnesia: Regional brain atrophy and its relationship to memory deficits. *Brain, 132*(2), 357-368.

Butler, C. R., Graham, K. S., Hodges, J. R., Kapur, N., Wardlaw, J. M., & Zeman, A. Z. J. (2007). The syndrome of transient epileptic amnesia. *Annals of Neurology, 61*(6), 587-598.

Butler, C. R., Kapur, N., Zeman, A., Weller, R., & Connelly, A. (2012). Epilepsy-related long-term amnesia: Anatomical perspectives. *Neuropsychologia*, *50,* 2973-2980.

Butler, C. R., van Erp, W., Bhaduri, A., Hammers, A., Heckemann, R., & Zeman, A. (2013). Magnetic resonance volumetry reveals focal brain atrophy in transient epileptic amnesia. *Epilepsy & Behaviour, 28*(3), 363-369.

Butler, C. R., & Zeman, A. Z. J. (2008). Recent insights into the impairment of memory in epilepsy: Transient epileptic amnesia, accelerated long-term forgetting and remote memory impairment. *Brain, 131*(9), 2243-2263.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28*(2), 193-213.

Canafoglia, L., Franceschetti, S., Antozzi, C., Carrara, F., Farina, L., Granata, T., . . . Villani, F. (2001). Epileptic phenotypes associated with mitochondrial disorders. *Neurology, 56*(10), 1340-1346.

Canivez, G. L., & Watkins, M. W. (2010). Investigation of the factor structure of the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS–IV): Exploratory and higher order factor analyses. *Psychological Assessment, 22*(4), 827-836.

Carrion, M. J. M., Nunes, M. L., Martinez, J. V. L., Portuguez, M. W., & da Costa, J. C. (2010). Evaluation of sleep quality in patients with refractory seizures who undergo epilepsy surgery. *Epilepsy & Behaviour, 17*(1), 120-123.

Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lönnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. *Journal of Affective Disorders, 106*(1), 1-27.

Chen, N.-C., Tsai, M.-H., Chang, C.-C., Lu, C.-H., Chang, W.-N., Lai, S.-L., . . . Chuang, Y.-C. (2011). Sleep quality and daytime sleepiness in patients with epilepsy. *Acta Neurologica Taiwanica, 20*(4), 249-256.

Cohen, G., Kiss, G., & LeVoi, M. (1993). *Memory: Current issues.* (2nd ed.). Buckingham: Open University Press.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112*(1), 155-199.

Corcoran, R., & Thompson, P. (1992). Memory failure in epilepsy: Retrospective reports and prospective recordings. *Seizure, 1*(1), 37-42.

Council, J. E. (2005). *Epilepsy prevalence, incidence and other statistics.* Leeds: Joint Epilepsy Council.

Crawford, J. R., & Henry, J. D. (2005). Assessment of executive dysfunction. In P.W. Halligan & D.T. Wade (Eds.), *Effectiveness of rehabilitation for cognitive deficits* (pp. 233-246). Oxford: Oxford University Press.

Cronel-Ohayon, S., Zesiger, P., Davidoff, V., Boni, A., Roulet, E., & Deonna, T. (2006). Deficit in memory consolidation (abnormal forgetting rate) in childhood temporal lobe epilepsy. Pre and postoperative long-term observation. *Neuropaediatrics, 37*(06), 317-324.

Crowley, S. (2014). *Accelerated long-term forgetting in epilepsy: Assessment using the WMS-IV with extended procedures.* Unpublished doctoral dissertation, University of East London, Stratford, London.

Dalgleish, T., & Watts, F. N. (1990). Biases of attention and memory in disorders of anxiety and depression. *Clinical Psychology Review, 10*(5), 589-604.

Davidson, M., Dorris, L., O'Regan, M., & Zuberi, S. M. (2007). Memory consolidation and accelerated forgetting in children with idiopathic generalized epilepsy. *Epilepsy & Behaviour, 11*(3), 394-400.

de Frias, C. M., Dixon, R. A., & Strauss, E. (2006). Structure of four executive functioning tests in healthy older adults. *Neuropsychology, 20*(2), 206-214.

De Renzi, E., & Lucchelli, F. (1993). Dense retrograde amnesia, intact learning capability and abnormal forgetting rate: A consolidation deficit? *Cortex, 29*(3), 449-466.

Deak, M. C., Stickgold, R., Pietras, A. C., Nelson, A. P., & Bubrick, E. J. (2011). The role of sleep in forgetting in temporal lobe epilepsy: A pilot study. *Epilepsy & Behaviour, 21*(4), 462-466.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System (D-KEFS)*. Virginia: The Psychological Corporation.

Delis, D. C., Kramer, J. H., Kaplan, E., & Holdnack, J. (2004). Reliability and validity of the Delis-Kaplan Executive Function System: An update. *Journal of the International Neuropsychological Society, 10*(02), 301-303.

Djordjevic, J., Smith, M. L., Sziklas, V., Piper, D., Pénicaud, S., & Jones-Gotman, M. (2011). The Story Learning and Memory (SLAM) test: Equivalence of three forms and sensitivity to left temporal lobe dysfunction. *Epilepsy & Behaviour, 20*(3), 518-523.

Doss, R. C., Chelune, G. J., & Naugle, R. I. (2004). WMS-III performance in epilepsy patients following temporal lobectomy. *Journal of the International Neuropsychological Society, 10*(02), 173-179.

Dow, C., Seidenberg, M., & Hermann, B. (2004). Relationship between information processing speed in temporal lobe epilepsy and white matter volume. *Epilepsy & Behaviour, 5*(6), 919-925.

Drozdick, L. W., Holdnack, J. A., & Hilsabeck, R. C. (2011). *Essentials of WMS-IV assessment* (Vol. 85). New York: John Wiley & Sons.

Dudai, Y. (2004). The neurobiology of consolidations, or, how stable is the engram? *Annual Review of Psychology, 55*, 51-86.

Duff, K., Schoenberg, M. R., Scott, J. G., & Adams, R. L. (2005). The relationship between executive functioning and verbal and visual learning and memory. *Archives of Clinical Neuropsychology, 20*(1), 111-122.

Dupont, S., Van de Moortele, P., Samson, S., Hasboun, D., Poline, J., Adam, C., . . . Baulac, M. (2000). Episodic memory in left temporal lobe epilepsy: A functional MRI study. *Brain, 123*(8), 1722-1732.

Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology, 25*, 117-129.

Ebbinghaus, H. (1885). *Memory: A contribution to experimental psychology.* New York: Dover.

Elliott, G., Isaac, C. L., & Muhlert, N. (2014). Measuring forgetting: A critical review of accelerated long-term forgetting studies. *Cortex, 54*, 16-32.

Elliott, I. M., Lach, L., & Smith, M. L. (2005). I just want to be normal: A qualitative study exploring how children and adolescents view the impact of intractable epilepsy on their quality of life. *Epilepsy & Behaviour, 7*(4), 664-678.

Evans, S. J., Elliott, G., Reynders, H., & Isaac, C. L. (2014). Can temporal lobe epilepsy surgery ameliorate accelerated long-term forgetting? *Neuropsychologia, 53*, 64-74.

Ferrier, J. F. (1854). *Institutes of metaphysics: The theory of knowing and being.* Edinburgh: Blackwood.

Fisher, R. S., Acevedo, C., Arzimanoglou, A., Bogacz, A., Cross, J. H., Elger, C. E., . . . Glynn, M. (2014). ILAE official report: A practical clinical definition of epilepsy. *Epilepsia, 55*(4), 475-482.

Fisher, R. S., Vickrey, B. G., Gibson, P., Hermann, B., Penovich, P., Scherer, A., & Walker, S. (2000). The impact of epilepsy from the patient's perspective I. Descriptions and subjective perceptions. *Epilepsy Research, 41*(1), 39-51.

Fitzgerald, Z., Mohamed, A., Ricci, M., Thayer, Z., & Miller, L. (2013). Accelerated long-term forgetting: A newly identified memory impairment in epilepsy. *Journal of Clinical Neuroscience, 20*(11), 1486-1491.

Fitzgerald, Z., Thayer, Z., Mohamed, A., & Miller, L. A. (2013). Examining factors related to accelerated long-term forgetting in epilepsy using ambulatory EEG monitoring. *Epilepsia, 54*(5), 819-827.

Flanagan, O. J. (1981). Psychology, progress, and the problem of reflexivity: A study in the epistemological foundations of psychology. *Journal of the History of the Behavioural Sciences, 17*(3), 375-386.

Flynn, J. R. (1987). Massive IQ gains in 14 nations: What IQ tests really measure. *Psychological Bulletin, 101*(2), 171-191.

Frankland, P. W., & Bontempi, B. (2005). The organization of recent and remote memories. *Nature Reviews Neuroscience, 6*(2), 119-130.

Gallassi, R., Sambati, L., Poda, R., Stanzani Maserati, M., Oppi, F., Giulioni, M., & Tinuper, P. (2011). Accelerated long-term forgetting in temporal lobe epilepsy: Evidence of improvement after left temporal pole lobectomy. *Epilepsy & Behaviour, 22*(4), 793-795.

Giovagnoli, A. R., Casazza, M., & Avanzini, G. (1995). Visual learning on a selective reminding procedure and delayed recall in patients with temporal lobe epilepsy. *Epilepsia, 36*(7), 704-711.

Glass, G. V., Peckham, P. D., & Sanders, J. R. (1972). Consequences of failure to meet assumptions underlying the fixed effects analyses of variance and covariance. *Review of Educational Research*, *42,* 237-288.

Hartman, D. E. (2009). Wechsler Adult Intelligence Scale-IV (WAIS-IV): Return of the gold standard. *Applied Neuropsychology, 16*(1), 85-87.

Helmstaedter, C., Hauff, M., & Elger, C. (1998). Ecological validity of list-learning tests and self-reported memory in healthy individuals and those with temporal lobe epilepsy. *Journal of Clinical and Experimental Neuropsychology, 20*(3), 365-375.

Helmstaedter, C., & Kurthen, M. (2011). Memory and epilepsy: Characteristics, course, and influence of drugs and surgery. *Current Opinion in Neurology, 14*(2), 211-116.

Hermann, B., & Seidenberg, M. (2007). Epilepsy and cognition. *Epilepsy Currents, 7*(1), 1-6.

Hermann, B., Seidenberg, M., Bell, B., Rutecki, P., Sheth, R., Ruggles, K., . . . Magnotta, V. (2002). The neurodevelopmental impact of childhood-onset temporal lobe epilepsy on brain structure and function. *Epilepsia, 43*(9), 1062-1071.

Hessen, E., Lossius, M. I., Reinvang, I., & Gjerstad, L. (2006). Influence of major antiepileptic drugs on attention, reaction time, and speed of information processing: Results from a randomized, double-blind, placebo-controlled withdrawal study of seizure-free epilepsy patients receiving monotherapy. *Epilepsia, 47*(12), 2038-2045.

Hirtz, D., Thurman, D., Gwinn-Hardy, K., Mohamed, M., Chaudhuri, A., & Zalutsky, R. (2007). How common are the “common” neurologic disorders? *Neurology, 68*(5), 326-337.

Hoefeijzers, S., Dewar, M., Della Sala, S., Zeman, A., & Butler, C. (2013). Accelerated long-term forgetting in transient epileptic amnesia: An acquisition or consolidation deficit? *Neuropsychologia, 51*(8), 1549-1555.

Hoelzle, J. B., Nelson, N. W., & Smith, C. A. (2011). Comparison of Wechsler Memory Scale Fourth Edition (WMS-IV) and Third Edition (WMS-III) dimensional structures: Improved ability to evaluate auditory and visual constructs. *Journal of Clinical and Experimental Neuropsychology, 33*(3), 283-291.

Holdnack, J. A., Zhou, X., Larrabee, G. J., Millis, S. R., & Salthouse, T. A. (2011). Confirmatory factor analysis of the WAIS-IV/WMS-IV. *Assessment, 18*(2), 178-191.

Homack, S., Lee, D., & Riccio, C. A. (2005). Test review: Delis-Kaplan Executive Function System. *Journal of Clinical and Experimental Neuropsychology, 27*(5), 599-609.

ILAE. (1989). Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia, 30*, 389-399.

Jacoby, A., & Austin, J. K. (2007). Social stigma for adults and children with epilepsy. *Epilepsia, 48*(9), 6-9.

Jansari, A. S., Davis, K., McGibbon, T., Firminger, S., & Kapur, N. (2010). When "long-term memory" no longer means "forever": Analysis of accelerated long-term forgetting in a patient with temporal lobe epilepsy. *Neuropsychologia, 48*(6), 1707-1715.

Johnson, D. H. (1999). The insignificance of statistical significance testing. *The Journal of Wildlife Management*, *63(3),* 763-772.

Jokeit, H., & Schacher, M. (2004). Neuropsychological aspects of type of epilepsy and etiological factors in adults. *Epilepsy & Behaviour, 5*, 14-20.

Jones-Gotman, M. (1993). Neuropsychological testing for localization and lateralization of the epileptogenic region. In J. Engel (Ed.), *Surgical treatment of the epilepsies* (pp. 245-261). New York: Raven Press.

Kapur, N., Millar, J., Colbourn, C., Abbott, P., Kennedy, P., & Docherty, T. (1997). Very long-term amnesia in association with temporal lobe epilepsy: Evidence for multiple-stage consolidation processes. *Brain and Cognition, 35*(1), 58-70.

Kapur, N., Scholey, K., Moore, E., Barker, S., Brice, J., Thompson, S., . . . Fleming, J. (1996). Long-term retention deficits in two cases of disproportionate retrograde amnesia. *Journal of Cognitive Neuroscience, 8*(5), 416-434.

Keller, S. S., Baker, G., Downes, J. J., & Roberts, N. (2009). Quantitative MRI of the prefrontal cortex and executive function in patients with temporal lobe epilepsy. *Epilepsy & Behaviour, 15*(2), 186-195.

Kemp, S., Illman, N., Moulin, C., & Baddeley, A. (2012). Accelerated long-term forgetting (ALF) and transient epileptic amnesia (TEA): Two cases of epilepsy-related memory disorder. *Epilepsy & Behaviour, 24*(3), 382-388.

Kinnunen, K. M., Greenwood, R., Powell, J. H., Leech, R., Hawkins, P. C., Bonnelle, V., . . . Sharp, D. J. (2010). White matter damage and cognitive impairment after traumatic brain injury. *Brain*, *134,* 449-463.

Ko, D. Y. (2014). *Temporal lobe epilepsy*. Retrieved from http://emedicine.medscape.com/article/1184509-overview

Kolb, B., & Whishaw, I. Q. (2009). *Fundamentals of human neuropsychology*. London: Palgrave Macmillan.

Kotila, M., & Waltimo, O. (1992). Epilepsy after stroke. *Epilepsia, 33*(3), 495-498.

Krishnan, P., Sinha, S., Taly, A. B., Ramachandraiah, C. T., Rao, S., & Satishchandra, P. (2012). Sleep disturbances in juvenile myoclonic epilepsy: A sleep questionnaire-based study. *Epilepsy & Behaviour, 23*(3), 305-309.

Lah, S., Mohamed, A., Thayer, Z., Miller, L., & Diamond, K. (2014). Accelerated long-term forgetting of verbal information in unilateral temporal lobe epilepsy: Is it related to structural hippocampal abnormalities and/or incomplete learning? *Journal of Clinical and Experimental Neuropsychology, 36*(2), 158-169.

Laidlaw, M. V., & Laidlaw, J. (1980). *Epilepsy explained*. London: Churchill Livingstone.

Lancman, M. E., & Morris, H. H. (1996). Epilepsy after central nervous system infection: Clinical characteristics and outcome after epilepsy surgery. *Epilepsy Research, 25*(3), 285-290.

Landauer, T. K. (1986). How much do people remember? Some estimates of the quantity of learned information in long-term memory. *Cognitive Science, 10*(4), 477-493.

Lechner, H. A., Squire, L. R., & Byrne, J. H. (1999). 100 years of consolidation - remembering Müller and Pilzecker. *Learning & Memory, 6*(2), 77-87.

Lezak, M., Howieson, D., Bigler, E., & Tranel, D. (2012). *Neuropsychological assessment*. (5th ed.). Oxford: Oxford University Press.

Loring, D. W., & Bauer, R. M. (2010). Testing the limits: Cautions and concerns regarding the new Wechsler IQ and memory scales. *Neurology, 74*(8), 685-690.

Lucchelli, F., & Spinnler, H. (1998). Ephemeral new traces and evaporated remote engrams: A form of neocortical temporal lobe amnesia? A preliminary case report. *Neurocase, 4*(6), 447-459.

Lunney, G. H. (1970). Using analysis of variance with a dichotomous dependent variable: An empirical study. *Journal of Educational Measurement, 7*(4), 263-269.

Mameniskiene, R., Jatuzis, D., Kaubrys, G., & Budrys, V. (2006). The decay of memory between delayed and long-term recall in patients with temporal lobe epilepsy. *Epilepsy & Behaviour, 8*(1), 278-288.

Manes, F., Graham, K. S., Zeman, A., Calcagno, M. d. L., & Hodges, J. R. (2005). Autobiographical amnesia and accelerated forgetting in transient epileptic amnesia. *Journal of Neurology, Neurosurgery & Psychiatry, 76*(10), 1387-1391.

Manning, L., Voltzenlogel, V., Chassagnon, S., Hirsch, E., Kehrli, P., & Maitrot, D. (2006). Selective memory impairment for public events associated with accelerated forgetting in a patient with left temporal lobe epilepsy. *Revue Neurologique, 162*(2), 222-228.

Martin, R. C., Loring, D. W., Meador, K. J., Lee, G. P., Thrash, N., & Arena, J. G. (1991). Impaired long-term retention despite normal verbal learning in patients with temporal lobe dysfunction. *Neuropsychology, 5*(1), 3-12.

Matlin, M. W. (2005). *Cognition*. New Jersey: Wiley.

Mayes, A. R., Isaac, C. L., Holdstock, J. S., Cariga, P., Gummer, A., & Roberts, N. (2003). Long-term amnesia: A review and detailed illustrative case study. *Cortex, 39*(4), 567-603.

McGibbon, T., & Jansari, A. S. (2013). Detecting the onset of accelerated long-term forgetting: Evidence from temporal lobe epilepsy. *Neuropsychologia, 51*(1), 114-122.

McGuire, P. K., Murray, R., & Shah, G. (1993). Increased blood flow in Broca's area during auditory hallucinations in schizophrenia. *The Lancet, 342*(8873), 703-706.

McLeod, S. A. (2007). *Stages of memory: Encoding, storage and retrieval.* Retrieved from http://www.simplypsychology.org/memory.html

Miller, G. A. (1956). The magical number seven, plus or minus two: Some limits on our capacity for processing information. *Psychological Review, 63*(2), 81-97.

Milner, B. (1971). Interhemispheric differences in the localization of psychological processes in man. *British Medical Bulletin, 27,* 272-277.

Morrell, M. J. (2002). Stigma and epilepsy. *Epilepsy & Behaviour, 3*(6), 21-25.

Muhlert, N., Grünewald, R. A., Hunkin, N. M., Reuber, M., Howell, S., Reynders, H., & Isaac, C. L. (2011). Accelerated long-term forgetting in temporal lobe but not idiopathic generalised epilepsy. *Neuropsychologia, 49*(9), 2417-2426.

Muhlert, N., Milton, F., Butler, C. R., Kapur, N., & Zeman, A. Z. (2010). Accelerated forgetting of real-life events in transient epileptic amnesia. *Neuropsychologia, 48*(11), 3235-3244.

Muslimović, D., Post, B., Speelman, J. D., & Schmand, B. (2005). Cognitive profile of patients with newly diagnosed Parkinson disease. *Neurology, 65*(8), 1239-1245.

Narayanan, J., Duncan, R., Greene, J., Leach, J.-P., Razvi, S., McLean, J., & Evans, J. J. (2012). Accelerated long-term forgetting in temporal lobe epilepsy: Verbal, nonverbal and autobiographical memory. *Epilepsy & Behaviour, 25*(4), 622-630.

Nelson, H. (1981). *The Nelson Adult Reading Rest (NART) manual.* Windsor: NFER-Nelson.

NICE. (2004). *The epilepsies: The diagnosis and management of the epilepsies in adults and children in primary and secondary care.* London: National Institute for Health and Care Excellence.

O'Connor, M., Sieggreen, M. A., Ahern, G., Schomer, D., & Mesulam, M. (1997). Accelerated forgetting in association with temporal lobe epilepsy and paraneoplastic encephalitis. *Brain and Cognition, 35*(1), 71-84.

Odhuba, R. A., Broek, M., & Johns, L. (2005). Ecological validity of measures of executive functioning. *British Journal of Clinical Psychology, 44*(2), 269-278.

Oyegbile, T., Dow, C., Jones, J., Bell, B., Rutecki, P., Sheth, R., . . . Hermann, B. (2004). The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. *Neurology, 62*(10), 1736-1742.

Pandolfo, M. (2011). Genetics of epilepsy. *Seminars in Neurology, 31*(5), 506-518.

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging, 17*(2), 299-320.

Parkin, A. J. (1993). *Memory: Phenomena, experiment and theory*. Hove: Psychology Press.

Piazzini, A., Canevini, M., Maggiori, G., & Canger, R. (2001). The perception of memory failures in patients with epilepsy. *European Journal of Neurology, 8*(6), 613-620.

Posner, M. I. (1966). Components of skilled performance. *Science, 152,* 1712-1718.

Randolph, C. (1998). *RBANS manual: Repeatable Battery for the Assessment of Neuropsychological Status.* San Antonio: The Psychological Corporation.

Richardson, A. (1993). The curious case of coins: Remembering the appearance of familiar objects. *The Psychologist, 6*(8), 249-253.

Ridsdale, L. (2009). The social causes of inequality in epilepsy and developing a rehabilitation strategy: A UK-based analysis. *Epilepsia, 50*(10), 2175-2179.

Robinson, P. (1995). Attention, memory, and the “noticing” hypothesis. *Language learning, 45*(2), 283-331.

Rogers, R. D., & Robbins, T. W. (2001). Investigating the neurocognitive deficits associated with chronic drug misuse. *Current Opinion in Neurobiology, 11*(2), 250-257.

Royle, J., & Lincoln, N. B. (2008). The Everyday Memory Questionnaire-Revised: Development of a 13-item scale. *Disability & Rehabilitation, 30*(2), 114-121.

Scambler, G. (1989). *Epilepsy: The experience of illness series.* London: Routledge.

Schmidt, M. (1996). *Rey Auditory Verbal Learning Test: A handbook*. Los Angeles: Western Psychological Services.

Sherman, E., Wiebe, S., Fay-McClymont, T. B., Tellez-Zenteno, J., Metcalfe, A., Hernandez-Ronquillo, L., . . . Jetté, N. (2011). Neuropsychological outcomes after epilepsy surgery: Systematic review and pooled estimates. *Epilepsia, 52*(5), 857-869.

Shunk, A. W., Davis, A. S., & Dean, R. S. (2006). Test review: Delis Kaplan Executive Function System (D-KEFS). *Applied Neuropsychology, 13*(4), 275-227.

Simioni, S., Cavassini, M., Annoni, J.-M., Abraham, A. R., Bourquin, I., Schiffer, V., . . . Hirschel, B. (2010). Cognitive dysfunction in HIV patients despite long-standing suppression of viremia. *Aids, 24*(9), 1243-1250.

Smeets, V. M., van Lierop, B. A., Vanhoutvin, J. P., Aldenkamp, A. P., & Nijhuis, F. J. (2007). Epilepsy and employment: Literature review. *Epilepsy & Behaviour, 10*(3), 354-362.

Smith, C. N., Frascino, J. C., Kripke, D. L., McHugh, P. R., Treisman, G. J., & Squire, L. R. (2010). Losing memories overnight: A unique form of human amnesia. *Neuropsychologia, 48*(10), 2833-2840.

Snaith, R. P. (2003). The hospital anxiety and depression scale. *Health and Quality of Life Outcomes, 1*(1), 29-33.

Squire, L. R. (2004). Memory systems of the brain: A brief history and current perspective. *Neurobiology of Learning and Memory, 82*(3), 171-177.

Squire, L. R., & Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. *Current Opinion in Neurobiology, 5*(2), 169-177.

Squire, L. R., & Zola-Morgan, S. (1991). The medial temporal lobe memory system. *Science, 253*(5026), 1380-1386.

Stewart, S. A. (2005). The effects of benzodiazepines on cognition. *Journal of Clinical Psychiatry*, *66*(2), 9-13.

Thurman, D. J., Beghi, E., Begley, C. E., Berg, A. T., Buchhalter, J. R., Ding, D., . . . Kobau, R. (2011). Standards for epidemiologic studies and surveillance of epilepsy. *Epilepsia, 52*(7), 2-26.

Tomlinson, T. D., Huber, D. E., Rieth, C. A., & Davelaar, E. J. (2009). An interference account of cue-independent forgetting in the no-think paradigm. *Proceedings of the National Academy of Sciences, 106*(37), 15588-15593.

Tramoni, E., Felician, O., Barbeau, E. J., Guedj, E., Guye, M., Bartolomei, F., & Ceccaldi, M. (2011). Long-term consolidation of declarative memory: Insight from temporal lobe epilepsy. *Brain, 134*(3), 816-831.

Tromp, S. C., Weber, J. W., Aldenkamp, A. P., Arends, J., vander Linden, I., & Diepman, L. (2003). Relative influence of epileptic seizures and of epilepsy syndrome on cognitive function. *Journal of Child Neurology, 18*(6), 407-412.

Tröster, A. I., Warmflash, V., Osorio, I., Paolo, A. M., Alexander, L. J., & Barr, W. B. (1995). The roles of semantic networks and search efficiency in verbal fluency performance in intractable temporal lobe epilepsy. *Epilepsy Research, 21*(1), 19-26.

Vedhara, K., Hyde, J., Gilchrist, I., Tytherleigh, M., & Plummer, S. (2000). Acute stress, memory, attention and cortisol. *Psychoneuroendocrinology, 25*(6), 535-549.

Vlooswijk, M., Jansen, J., Majoie, H., Hofman, P., de Krom, M., Aldenkamp, A., & Backes, W. (2010). Functional connectivity and language impairment in cryptogenic localization-related epilepsy. *Neurology, 75*(5), 395-402.

Walker, M. P., & Stickgold, R. (2006). Sleep, memory and plasticity. *Annual Review of Psychology, 57*, 139-166.

Wechsler, D. (1997). *Wechsler Memory Scale: WMS-III; Administration and scoring manual.* San Antonio: The Psychological Corporation.

Wechsler, D. (2009). *Wechsler Memory Scale: WMS-IV; Technical and interpretive manual*. San Antonio: Pearson Assessment.

Wechsler, D. (2010a). *Wechsler Adult Intelligence Scale - Fourth UK Edition*. London: Pearson Assessment.

Wechsler, D. (2010b). *Wechsler Memory Scale - Fourth UK Edition*. London: Pearson Assessment.

Wechsler, D. (2011). *Test of Premorbid Functioning - UK Version*. London: Pearson Assessment.

World Health Organisation (WHO). (2009). *Epilepsy fact sheet.* Retrieved from http://www.who.int/mediacentre/factsheets/fs999/en/index.html

Wiebe, S. (2000). Epidemiology of temporal lobe epilepsy. *The Canadian Journal of Neurological Sciences, 27*(1), 6-10.

Wiebe, S., Blume, W. T., Girvin, J. P., & Eliasziw, M. (2001). A randomized, controlled trial of surgery for temporal-lobe epilepsy. *New England Journal of Medicine, 345*(5), 311-318.

Wilde, N., Strauss, E., Chelune, G. J., Hermann, B. P., Hunter, M., Loring, D. W., . . . Sherman, E. (2003). Confirmatory factor analysis of the WMS-III in patients with temporal lobe epilepsy. *Psychological Assessment, 15*(1), 56-63.

Wilde, N., Strauss, E., Chelune, G. J., Loring, D. W., Martin, R. C., Hermann, B. P., . . . Hunter, M. (2001). WMS–III performance in patients with temporal lobe epilepsy: Group differences and individual classification. *Journal of the International Neuropsychological Society, 7*(07), 881-891.

Wilkinson, H., Holdstock, J. S., Baker, G., Herbert, A., Clague, F., & Downes, J. J. (2012). Long-term accelerated forgetting of verbal and non-verbal information in temporal lobe epilepsy. *Cortex, 48*(3), 317-332.

Williamson, P., Thadani, V., Darcey, T., Spencer, D., Spencer, S., & Mattson, R. (1992). Occipital lobe epilepsy: Clinical characteristics, seizure spread patterns, and results of surgery. *Annals of Neurology, 31*(1), 3-13.

Willig, C. (2012). Perspectives on the epistemological bases for qualitative research. In H. Cooper (Ed.), *The handbook of research methods in psychology* (pp. 5-21). Washington: American Psychological Association.

Wood, R. L., & Liossi, C. (2006). The ecological validity of executive tests in a severely brain injured sample. *Archives of Clinical Neuropsychology, 21*(5), 429-437.

Zhang, Z., Lu, G., Zhong, Y., Tan, Q., Yang, Z., Liao, W., . . . Liu, Y. (2009). Impaired attention network in temporal lobe epilepsy: A resting FMRI study. *Neuroscience Letters, 458*(3), 97-101.

Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale (HADS). *Acta Psychiatrica Scandinavica, 67*(6), 361-370.

APPENDIX 1 - ALF IN TLE: CASE STUDIES

Author/s (year)	Initials	Age (yrs)	Sex	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Cronel-Ohayon et al. (2006)	JE	18	M	L	Mild	- RAVLT words list recall (+) - CMS story recall (+) - CMS word pair recall (+)	- ROCFT figure recall (+)	1 week
Gallassi et al. (2011)	MT	58	M	L	No	- RAVLT word list recall (+) - Babcock story recall (-)	- RCFT recall (+)	1 week
Jansari et al. (2010)	RY	63	M	R	No	- WMS-R story recall Repeated (-) Non-repeated (+) - WMS-R story recognition Repeated (-) Non-repeated (+)	X	24 hours

(+)=ALF; (-)=No ALF; CMS=Children's Memory Scale; n/d=not discussed; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 1 (CONTINUED) - ALF IN TLE: CASE STUDIES

Author/s (year)	Initials	Age (yrs)	Sex	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Kapur et al. (1997)	PA	62	F	L	No	- WMS-R story recall (+) - WMS-R story recognition (+)	- WMS-R figure recall (+) - WMS-R figure recognition (-)	6 weeks
Kemp et al. (2012)	SK	37	M	Bilateral	Autobio-graphical memory	- WMS-III story recall (+) - WMS-III story recognition (+)	- WMS-III family pictures recall (+)	4 days
Lucchelli & Spinnler (1998)	GB	65	M	L	Mild verbal	- Babcock story recall (+)	- ROCFT figure recall (-)	1 week
Manning et al. (2006)	JR	54	M	L	No	- Novel story recall (+)	- Novel face recognition (+)	30 hours

(+)=ALF; (-)=No ALF; CMS=Children's Memory Scale; n/d=not discussed; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 1 (CONTINUED) - ALF IN TLE: CASE STUDIES

Author/s (year)	Initials	Age (yrs)	Sex	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Mayes et al. (2003)	JL	46	F	n/d	Face recognition	- Novel story recall (+) - Novel story recognition (+) - Novel word recognition (+)	- ROCFT figure recall (+) - ROCFT figure recognition (+) - Novel face recognition (+)	3 weeks
McGibbon & Jansari (2013)	RY	66	M	R	No	- WMS-R word pair recall Repeated (+) Non-repeated (-) - WMS-R word pair recognition Repeated (+) Non-repeated (-)	X	55 minutes
O'Connor et al. (1997)	JT	42	M	Bilateral	No	- Novel word list recall (+)	X	8 hours

(+)=ALF; (-)=No ALF; CMS=Children's Memory Scale; n/d=not discussed; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Bell et al. (2005)	42/49	R 40 (9.8); L 34 (13)	22 L; 20 R	Yes	- SRT word list recall (-)	- SRT design recall (-)	X
Bell (2006)	25/25	39 (10)	11 L; 6 R	Yes	- WMS-III story recall (-) - WMS-III story recognition (-)	X	X
Bengner et al. (2006)	56/12	39.2 (11.8)	20 L; 24 R	Yes	X	- Novel face recognition (+)	24 hours
Blake et al. (2000)	21/16	33.76 (9.7)	11 L; 10 R	No	- AMIPB story recall (+) - AMIPB story recognition (+)	X	8 weeks

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Butler et al. (2007)	24/24	68 (8.7)	8 L; 6 R; 4 bilateral; 16 slow-wave; 15 n/k	No	- RAVLT word list recall (+)	- ROCFT figure recall (+)	1 week
Butler et al. (2009)	22/20	66.4 (8.8)	n/d	No	- RAVLT word list recall - RMBT story recall - Combined analysis (+)	- Graham-Kendall Memory for Designs figure recall (+)	1 week
Butler et al. (2012)	22/20	66.4 (8.8)	n/d	Yes	- RAVLT word list recall (+)	X	1 week

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Butler et al. (2013)	22/20	66.4 (8.8)	n/d	No	- RAVLT word list recall (+)	- Graham-Kendall Memory for Designs figure recall (+)	1 week
Deak et al. (2011)	6/9	44 (n/d)	n/d	No	- SRT word list recall (+)	X	12 hours
Djordjevic et al. (2011)	90/19	L 33.5 (n/d); R 36.8 (n/d)	46 L; 44 R	Yes L; No R	- SLAM (+)	X	24 hours

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Evans et al. (2014)	7/25	39.71 (15.77)	3 L; 4 R	Yes	- Novel story recall (+) - Novel story recognition (+)	- Novel scene recall (+) - Novel scene recognition (-)	1 week
Fitzgerald et al. (2013)	39/15	n/d	n/d	No	- Novel word list recall (+)	- Novel figure recall (+)	4 days
Giovagnoli et al. (1995)	24/25	38 (11.6)	12 L; 12 R	No	X	- SRT figure recall (-)	X
Helmstaedter et al. (1998)	55/21	26.9 (n/d)	28 L; 27 R	Yes	- VLMT word list recall (+)	- DCS-R figure recall (+)	1 week

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Hoefeijzers et al. (2013)	24/24	65.47 (8.79)	n/d	No	- RAVLT word list recall (+)	X	1 week
Lah et al. (2014)	23/27	44.85 (26.8)	10 L; 13 R	No	- HVLT-R word list recall (+)	X	1 day
Mamenisk-iene et al. (2006)	70/59	33 (9.5)	n/d	Yes	- RAVLT word list recall (+) - VLS story recall (+)	- ROCFT figure recall (+)	4 weeks
Manes et al. (2005)	7/7	57 (8.1)	6 bilateral; 1 normal EEG	No	- WMS-R story recall (+) - WMS-R story recognition (+)	- WMS-R figure recall (+) - WMS-R figure recognition (+)	6 weeks

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Martin et al. (1991)	21/21	31 (7.5)	13 L; 8 R	No	- SRT word list recall (+)	X	24 hours
Muhlert et al. (2010)	11/11	68.9 (9.9)	n/d	No	- AMIPB word list recall (+)	- Real life SenseCam (+)	24 hours
Muhlert et al. (2011)	28/15	46.4 (11)	n/d	No	- Novel story recall (-) - Novel story recognition (+)	- Novel visual scenes Item recall (+) Descriptive recall (+) Spatial recall (-)	3 weeks
Narayanan et al. (2012)	14/17	33.57 (10.13)	9L; 6R	Yes	- RAVLT (+)	- ROCFT (-) - Labyrinth maze (-)	4 weeks

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 2 (CONTINUED) - ALF IN TLE: GROUP STUDIES

Author/s (year)	Number of TLE / Controls	TLE Mean Age (SD)	Seizure Laterality	Memory Impairment at 30 minutes	Measures of Verbal Extended Retrieval	Measures of Visual Extended Retrieval	First Long Delay with ALF
Tramoni et al. (2011)	5/15	42.6 (9.3)	1 L; 2 R; 2 bilateral	No	- Novel stories (+) - Facts (-) - Single-items (-)	- Routes (+) - Chain of episodes (+)	6 weeks
Wilkinson et al. (2011)	27/22	L 34.8 (10.1); R 38.7 (8.1)	15 L; 12 R	n/d	- WMS-III story recall (+)	- RCFT recall (+)	1 hour

(+)=ALF; (-)=No ALF; AMIPB=Adult Memory and Information Processing Battery; DCS-R=Diagnostikum fur Cerebralschaldi; EEG=electroencephalograph; HVLT-R=Hopkins Verbal Learning Test-Revised; n/d=not discussed; n/k=not known; RAVLT=Rey's Auditory Verbal Learning Test; ROCFT=Rey-Osterrieth's Complex Figure Test; RBMT=Rivermead Behavioural Memory Test; SLAM=Story Learning & Memory Test; SRT=Selective Reminding Test; VLMT=Verbal Learning and Memory Test; VLS=Verbal Logical Story; WMS-R=Wechsler Memory Scale-Revised; WMS-III=Wechsler Memory Scale-Third Edition

APPENDIX 3 - CONFIRMATION OF UEL RESEARCH REGISTRATION

[redacted]

17 June 2014

Student Number: [redacted]

Dear [redacted]

Registration as a Candidate for the University's Research Degree

I am pleased to inform you that the Research Degrees Subcommittee on behalf of the University Quality and Standards Committee, has registered you for the degree of Professional Doctorate.

Title of Professional Doctorate: Professional Doctorate in Clinical Psychology

Director of Studies: [redacted]

Supervisor/s: [redacted]

Registered Thesis Title: Accelerated Long-term forgetting in temporal lobe epilepsy: The WMS-IV, detection and effects of repetition.

Expected completion: According to your actual date of registration, which is **1 October 2013**, the registration period is as follows:

Minimum 18 months maximum 48 months (4 years), according to a full time mode of study.

Your thesis is therefore due to be submitted between:

1 April 2015 – 1 October 2017

I wish you all the best with your intended research degree programme. Please contact me if you have any further queries regarding to this matter.

Yours sincerely,

[redacted]

[redacted]
School Research Degrees Leader
Direct line: [redacted]
Email: [redacted]

Cc: [redacted]

APPENDIX 4 - CONFIRMATION OF UEL ETHICAL APPROVAL

ETHICAL PRACTICE CHECKLIST (Professional Doctorates)

SUPERVISOR: [redacted] **ASSESSOR:** [redacted]

STUDENT: [redacted] **DATE (sent to assessor):** 03/02/2014

Proposed research topic: Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy: The WMS-IV, Detection and Effects of Repetition *(working title)*

**Abbreviations: TLE – Temporal Lobe Epilepsy; ALF – Accelerated Long-Term Forgetting; WMS-IV – Wechsler Memory Scale: Fourth Edition.*

Course: Professional Doctorate in Clinical Psychology

1. Will free and informed consent of participants be obtained?	YES
2. If there is any deception is it justified?	N/A
3. Will information obtained remain confidential?	YES
4. Will participants be made aware of their right to withdraw at any time?	YES
5. Will participants be adequately debriefed?	YES
6. If this study involves observation does it respect participants' privacy?	NA
7. If the proposal involves participants whose free and informed consent may be in question (e.g. for reasons of age, mental or emotional incapacity), are they treated ethically?	NA
8. Is procedure that might cause distress to participants ethical?	NA
9. If there are inducements to take part in the project is this ethical?	NA
10. If there are any other ethical issues involved, are they a problem?	NO

APPROVED

YES

Assessor initials: [redacted] Date: 03/01/14

APPENDIX 4 (CONTINUED) - CONFIRMATION OF UEL ETHICAL APPROVAL

RESEARCHER RISK ASSESSMENT CHECKLIST (BSc/MSc/MA)

SUPERVISOR: [redacted] **ASSESSOR:** [redacted]

STUDENT: [redacted] **DATE (sent to assessor):** 03/02/2014

Proposed research topic: Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy: The WMS-IV, Detection and Effects of Repetition *(working title)*

**Abbreviations: TLE – Temporal Lobe Epilepsy; ALF – Accelerated Long-Term Forgetting; WMS-IV – Wechsler Memory Scale: Fourth Edition.*

Course: Professional Doctorate in Clinical Psychology

Would the proposed project expose the researcher to any of the following kinds of hazard?

1	Emotional	NO
2.	Physical	NO
3.	Other (e.g. health & safety issues)	NO

If you've answered YES to any of the above please estimate the chance of the researcher being harmed as: HIGH / MED / LOW

APPROVED

YES

Assessor initials: [redacted] Date: 03/01/14

For the attention of the assessor: Please return the completed checklists by e-mail to ethics.applications@uel.ac.uk within 1 week.

APPENDIX 4 (CONTINUED) - CONFIRMATION OF UEL ETHICAL APPROVAL

SCHOOL OF PSYCHOLOGY
Dean: Professor Mark N. O. Davies, PhD, CPsychol, CBiol.

UEL University of East London
www.uel.ac.uk

School of Psychology

Professional Doctorate Programmes

To Whom It May Concern:

This is to confirm that the Professional Doctorate candidate named in the attached ethics approval is conducting research as part of the requirements of the Professional Doctorate programme on which he/she is enrolled.

The Research Ethics Committee of the School of Psychology, University of East London, has approved this candidate's research ethics application and he/she is therefore covered by the University's indemnity insurance policy while conducting the research. This policy should normally cover for any untoward event. The University does not offer 'no fault' cover, so in the event of an untoward occurrence leading to a claim against the institution, the claimant would be obliged to bring an action against the University and seek compensation through the courts.

As the candidate is a student of the University of East London, the University will act as the sponsor of his/her research. UEL will also fund expenses arising from the research, such as photocopying and postage.

Yours faithfully,

[redacted]

Chair of the School of Psychology Ethics Sub-Committee

Stratford Campus, Water Lane, Stratford, London E15 4LZ
tel: +44 (0)20 8223 4966 fax: +44 (0)20 8223 4937
e-mail: mno.davies@uel.ac.uk web: www.uel.ac.uk/psychology

APPENDIX 5 - CONFIRMATION OF NHS ETHICAL APPROVAL

NHS
Health Research Authority
NRES Committee London - Camden & Islington
North East REC Office
Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
Tyne & Wear
NE32 3DT

Telephone: 0191 4283548

27 November 2013

[redacted]
University of East London
School of Psychology
Water Lane
London
E15 4LZ

Dear [redacted]

Study title:	**Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy: Assessment using the WMS-IV with Extended Procedures**
REC reference:	**13/LO/1582**
Protocol number:	**N/A**
IRAS project ID:	**130772**

Thank you for your letter of 08 November 2013, 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.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator [redacted]

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 site

APPENDIX 5 (CONTINUED) - CONFIRMATION OF NHS ETHICAL APPROVAL

NHS sites

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

Conditions of the favourable opinion

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

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

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

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

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact [redacted] the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

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

Approved documents

APPENDIX 5 (CONTINUED) - CONFIRMATION OF NHS ETHICAL APPROVAL

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

Document	*Version*	*Date*
Evidence of insurance or indemnity	[redacted] UMR B1262FI015 3413	29 July 2013
Investigator CV	[redacted]	
Investigator CV	[redacted]	08 August 2013
Letter from Sponsor	[redacted]	
Participant Consent Form: People with Epilepsy	2.2	11 July 2013
Participant Consent Form: Controls	2.2	11 July 2013
Participant Information Sheet: People with Epilepsy	2.4	07 November 2013
Participant Information Sheet: Controls	2.4	07 November 2013
Protocol	2.1	24 September 2013
Questionnaire: Neuropsychological Battery Instructions	2.0	18 September 2013
Questionnaire: Neuropsychological Better Record Forms	2	18 September 2013
Questionnaire: WMS-IV Instructions		
Questionnaire: WMS-IV Record Form		
Questionnaire: Long Delay Instructions		
Questionnaire: Long Delay Record Forms		
REC application	IRAS Version 3.5, 130772/505377/1/980	25 September 2013
Response to Request for Further Information	[redacted]	08 November 2013

Statement of compliance

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

After ethical review

Reporting requirements

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

- Notifying substantial amendments
- Adding new sites and investigators

APPENDIX 5 (CONTINUED) - CONFIRMATION OF NHS ETHICAL APPROVAL

- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

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

Feedback

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

Further information is available at National Research Ethics Service website > After Review

13/LO/1582	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely

pp

[redacted]
Chair

Email: nrescommittee.london-camdenandislington@nhs.net

Enclosures: "After ethical review – guidance for researchers"

Copy to: [redacted]

APPENDIX 6 - CONFIRMATION OF NHS R&D APPROVAL

Queen Mary University of London

Barts Health NHS Trust

Joint Research Management Office
Queen Mary Innovation Centre
5 Walden Street
London
E1 2EF

Tel: 020 7882 7260
Fax: 020 7882 7276
Email: Sponsorsrep@bartshealth.nhs.uk

FINAL R&D APPROVAL

09 December 2013

[redacted]
Barts Health NHS Trust
Royal London Hospital
Whitechapel Road
Whitechapel,
London
United Kingdom
E1 1BB

Dear [redacted]

Protocol: **Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy: Assessment using the WMSIV with Extended Procedures**

ReDA Ref: **009352**
REC Ref: **13/LO/1582**

I am pleased to inform you that the Joint Research Management Office for Barts Health NHS Trust and Queen Mary University of London has approved the above referenced study and in so doing has ensured that there is appropriate indemnity cover against any negligence that may occur during the course of your project. Approved study documents are as follows:

Type	Version	Date
Protocol	2.1	September 2013
Neuropsychological Battery: Test order and instructions	2.0	18 September 2013
Neuropsychological Battery: Record Form	2	18 September 2013
Participant Consent Form (Controls)	2.2	11 July 2013
Participant Consent Form	2.2	11 July 2013
Participant Information Sheet (Controls)	2.4	07 November 2013
Participant Information Sheet	2.4	07 November 2013
Long Delay WMS Instructions		
Long Delay Record Forms		
WMS –IV Adult Battery Record Form		
WMS –IV Instructions		

Please note that all research within the NHS is subject to the Research Governance Framework for Health and Social Care, 2005. If you are unfamiliar with the standards contained in this document, or the BH and QMUL policies that reinforce them, you can obtain details from the Joint Research Management Office or go to:
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

APPENDIX 6 (CONTINUED) - CONFIRMATION OF NHS R&D APPROVAL

You must stay in touch with the Joint Research Management Office during the course of the research project, in particular:

- If there is a change of Principal Investigator
- When the project finishes
- If amendments are made, whether substantial or non-substantial

This is necessary to ensure that your R&D Approval and indemnity cover remain valid. Should any Serious Adverse Events (SAEs) or untoward events occur it is **essential** that you inform the Sponsor within 24 hours. If patients or staff are involved in an incident, you should also follow the Trust Adverse Incident reporting procedure or contact the Risk Management Unit on 020 7480 4718.

We wish you all the best with your research, and if you need any help or assistance during its course, please do not hesitate to contact the Office.

Yours sincerely

[redacted]

Copy to: Sponsor Organisation

APPENDIX 7 - RLH TLE GROUP CONSENT FORM

Barts Health NHS
NHS Trust

CONSENT FORM

Title of Study: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

Please Tick:

1. I confirm that I have read and understand the information sheet dated 07/11/2013 (version 2.4.) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that data collected during the study may be looked at by individuals from the University of East London, from regulatory authorities or from the NHS Trust, where this is necessary. Identifiable information will be kept confidential. I give permission for these individuals to have access to this information. ☐
4. I agree to take part in the above study. ☐

I would like to receive a summary of the results of the research when completed (*please circle)*: YES / NO

If YES, contact details (address or email): .....
.....

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

* When completed: 1 for participant; 1 for researcher site file.

11/07/2013 Version 2.2.

APPENDIX 8 - EA TLE GROUP CONSENT FORM

CONSENT FORM

Title of Study: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

Please Tick:

1. I confirm that I have read and understand the information sheet dated 04/11/2014 (version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that data collected during the study may be looked at by individuals from the University of East London, from regulatory authorities or from the NHS Trust, where this is necessary. Identifiable information will be kept confidential. I give permission for these individuals to have access to this information. ☐
4. I agree to take part in the above study. ☐

I would like to be provided with a **summary report of the neuropsychological assessment** (*please circle*): YES / NO

I would like to receive a summary of the results of the research when completed (*please circle*): YES / NO

If YES, contact details (address or email): .....
.....

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

* When completed: 1 for participant; 1 for researcher site file.

04/11/2014 Version 1

APPENDIX 9 - CONTROL GROUP CONSENT FORM

Barts Health NHS
NHS Trust

CONSENT FORM

Title of Study: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

Please Tick:

1. I confirm that I have read and understand the information sheet dated 07/11/2013 (version 2.4.) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that data collected during the study may be looked at by individuals from the University of East London, from regulatory authorities or from the NHS Trust, where this is necessary. Identifiable information will be kept confidential. I give permission for these individuals to have access to this information. ☐
4. I agree to take part in the above study. ☐

I would like to receive a summary of the results of the research when completed (*please circle)*: YES / NO

If YES, contact details (address or email): .....
.....

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher	Date	Signature

* When completed: 1 for participant; 1 for researcher site file.

11/07/2013 Version 2.2.

APPENDIX 10 - RLH TLE GROUP INVITATION LETTER

Barts Health NHS
NHS Trust

PARTICIPANT INFORMATION SHEET

Project Title: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. **One of our team will go through the information sheet with you and answer any questions you have.** We'd suggest this should take about 5-10 minutes. Please ask us if there is anything that is not clear.

What is the purpose of the study?
The aim of this study is to look at new ways of measuring memory difficulties in people with epilepsy. It will use a reliable and commonly used assessment tool along with some additional measures to look at a range of areas such as memory, attention, and information processing. The results will be compared to data from a group of people who do not have epilepsy to look at the similarities and differences and identify whether this is a reliable way to measure for memory difficulties.

Why have I been invited?
People with epilepsy who are attending the Neurology Service at the Royal London Hospital are invited to take part. You do not need to have any problems with memory. We are interested to compare the differences between those who do and do not report memory problems. Your contribution is important to us and we would like as many people as possible to take part.

Do I have to take part?
It is up to you to decide to join the study, your participation is voluntary. You are free to withdraw at any time, without giving a reason. There will be no consequences to the quality of care you receive. If you decide to withdraw, then any data we have collected about you will be destroyed.

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential and held securely, following ethical and legal practice. All data collected will be anonymised using a client ID number.

What will I be asked to do if I take part?
You will be asked to complete a set of psychological tasks exploring a wide range of abilities, for example, memory, problem-solving and understanding. The tasks will involve a mixture of verbal responses and pen-and-paper exercises. It will take approximately 1 hour and 30 minutes in total, including at least one break in the middle.

After the assessment, we will arrange a follow-up appointment one week later where you will be asked to take part in some more short assessment tasks. We will also give you a summary of the results and answer any questions or queries you have. The follow-up appointment will last a maximum of 30 minutes.

APPENDIX 10 (CONTINUED) - RLH TLE GROUP INVITATION LETTER

Expenses and Payments
You will be reimbursed for any public travel or petrol costs as a result of taking part in this research. Please talk to the researcher to arrange this.

What are the alternatives for diagnosis and treatment?
If you are worried about memory problems or any other cognitive difficulties, but you do not want to take part in the research, then you can ask your consultant to be referred for an assessment. Our research assessment takes approximately 10-15 minutes longer than a standard assessment due to the additional memory tasks that are included.

What are the possible disadvantages and risks of taking part?
There are no known risks to taking part. If you feel tired at any time during the assessment, we can stop and/or take a break. Neither the questions nor procedures are in anyway harmful.

What are the possible benefits of taking part?
In the same way as if you were referred for a standard cognitive assessment, we will offer to write a summary of your results for you and your consultant which may support further treatment. We will only do this if you give your consent.

Your participation will contribute to help clinicians and epilepsy patients to better understand memory problems. The results of the study will also potentially assist further research in this area and the development of strategies for early detection and management of memory difficulties.

You can request to have a summary of the research findings. If you would like a summary then you will be asked to give some contact details so that we may send this to you.

What will happen to the results of the research study?
The results obtained from this research will be incorporated into a doctoral thesis that will be submitted to the University of East London. The thesis may be published in an academic journal, however any identifiable data about you will not be included in any report or publication.

Further Information:
Please feel free to ask the researcher any questions. If you are happy to continue you will be asked to sign a consent form prior to your participation. Please retain this invitation letter for reference.

What if there is a problem?
If you have any concerns about any aspect of this study, you should contact the Principal Investigator, who will do their best to answer your questions. If you remain unhappy and wish to complain formally, please contact the Research Supervisor [redacted] or the Chair of the School of Psychology Research Ethics Sub-committee.

Contact Details:

Principal Investigator:
[redacted]

Research Supervisor:
[redacted]

Chair of the School of Psychology Research Ethics Sub-committee
[redacted]

07/11/2013 Version 2.4.

APPENDIX 11 - EA TLE GROUP INVITATION LETTER

PARTICIPANT INFORMATION SHEET

Project Title: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. **One of our team will go through the information sheet with you and answer any questions you have.** We'd suggest this should take about 5-10 minutes. Please ask us if there is anything that is not clear.

What is the purpose of the study?
The aim of this study is to look at new ways of measuring memory difficulties in people with epilepsy. It will use a reliable and commonly used assessment tool along with some additional measures to look at a range of areas such as memory, attention, and information processing. The results will be compared to data from a group of people who do not have epilepsy to look at the similarities and differences and identify whether this is a reliable way to measure for memory difficulties.

Why have I been invited?
People with a diagnosis of Temporal Lobe Epilepsy are invited to take part. You do not need to have any problems with memory. We are interested to compare the differences between those who do and do not report memory problems. Your contribution is important to us and we would like as many people as possible to take part.

Do I have to take part?
It is up to you to decide to join the study, your participation is voluntary. You are free to withdraw at any time, without giving a reason. There will be no consequences to the quality of care you receive. If you decide to withdraw, then any data we have collected about you will be destroyed.

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential and held securely, following ethical and legal practice. All data collected will be anonymised using a client ID number.

What will I be asked to do if I take part?
You will be asked to complete a set of psychological tasks exploring a wide range of abilities, for example, memory, problem-solving and understanding. The tasks will involve a mixture of verbal responses and pen-and-paper exercises. It will take approximately 1 hour and 30 minutes in total, including at least one break in the middle.

After the assessment, we will arrange a follow-up appointment one week later where you will be asked to take part in some more short assessment tasks. The follow-up appointment will last a maximum of 30 minutes.

Expenses and Payments
You will be reimbursed for any public travel or petrol costs as a result of taking part in this research. Please talk to the researcher to arrange this.

04/11/2014 Version 1

APPENDIX 11 (CONTINUED) - EA TLE GROUP INVITATION LETTER

What are the alternatives for diagnosis and treatment?
If you are worried about memory problems or any other cognitive difficulties, but you do not want to take part in the research, then you can ask your GP to be referred for an assessment. Our research assessment takes approximately 10-15 minutes longer than a standard assessment due to the additional memory tasks that are included.

What are the possible disadvantages and risks of taking part?
There are no known risks to taking part. If you feel tired at any time during the assessment, we can stop and/or take a break. Neither the questions nor procedures are in anyway harmful.

What are the possible benefits of taking part?
In the same way as if you were referred for a standard cognitive assessment, we will offer to write a summary of your results for you. This will include information about your memory, attention and processing speed, visuo-spatial and language functioning. The summary will include any areas of relative strength and/or weakness that you may be experiencing in cognitive function, and if any difficulties are detected we will also be able to provide you with some recommendations. If necessary we will offer to refer you onto appropriate services for support with any difficulties that you may be experiencing, and/or to provide a clinical report to your GP to support accessing appropriate services. We will only do this if you give your consent.

Your participation will contribute to help clinicians and epilepsy patients to better understand memory problems. The results of the study will also potentially assist further research in this area and the development of strategies for early detection and management of memory difficulties.

You can request to have a summary of the research findings. If you would like a summary then you will be asked to give some contact details so that we may send this to you.

What will happen to the results of the research study?
The results obtained from this research will be incorporated into a doctoral thesis that will be submitted to the University of East London. The thesis may be published in an academic journal, however any identifiable data about you will not be included in any report or publication.

Further Information:
Please feel free to ask the researcher any questions. If you are happy to continue you will be asked to sign a consent form prior to your participation. Please retain this invitation letter for reference.

What if there is a problem?
If you have any concerns about any aspect of this study, you should contact the Principal Investigator, who will do their best to answer your questions. If you remain unhappy and wish to complain formally, please contact the Research Supervisor [redacted] or the Chair of the School of Psychology Research Ethics Sub-committee.

Contact Details:

Principal Investigator:
[redacted]

Research Supervisor:
[redacted]

Chair of the School of Psychology Research Ethics Sub-committee
[redacted]

04/11/2014 Version 1

APPENDIX 12 - EA TLE GROUP ADVERTISEMENT

Research Study:
Memory and Temporal Lobe Epilepsy

We are asking people with a diagnosis of Temporal Lobe Epilepsy (TLE) to take part in a research study looking at memory in people with epilepsy.

We will ask you to undertake tests of

learning & memory
attention and information processing
language and perception
problem-solving

Testing will be over two sessions, which will be held 7 days apart.
The first session will take approximately 1 hour 30 minutes (including at least one break in the middle).
The second session will take no more than 30 minutes.

In return, (with your permission) we can

provide you with a summary of your results
and if you are experiencing any difficulties

- provide you with recommendations
- refer you onto appropriate services for additional support
- provide a report to your GP to support accessing appropriate services

To take part you must

be aged 18 years or older
fluent in English
be able to attend and take part in cognitive testing

If you are interested, please contact me directly

[redacted]

Thank you

APPENDIX 13 - CONTROL GROUP INVITATION LETTER

Barts Health NHS
NHS Trust

PARTICIPANT INFORMATION SHEET

Project Title: Investigating the Utility of the WMS-IV^{UK} with Novel Procedures as an Assessment Tool for Accelerated Long-Term Forgetting in Temporal Lobe Epilepsy

Principal Investigator: [redacted], Trainee Clinical Psychologist

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. **One of our team will go through the information sheet with you and answer any questions you have.** We'd suggest this should take about 5-10 minutes. Please ask us if there is anything that is not clear.

What is the purpose of the study?
The aim of this study is to look at new ways of measuring memory difficulties in people with epilepsy. It will use a reliable and commonly used assessment tool along with some additional measures to look at a range of areas such as memory, attention, and information processing. The results need to be compared to data from a group of people who do not have epilepsy to look at the similarities and differences and identify whether this is a reliable way to measure for memory difficulties.

Why have I been invited?
We are asking people from the general population to take part as a participant in our comparison group. Your contribution is important to us and we would like as many people as possible to take part.

Do I have to take part?
It is up to you to decide to join the study, your participation is voluntary. You are free to withdraw at any time, without giving a reason and without consequence. If you decide to withdraw, then any data we have collected about you will be destroyed.

Will my taking part in the study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential and held securely, following ethical and legal practice. All data collected will be anonymised using a client ID number.

What will I be asked to do if I take part?
You will be asked to complete a set of psychological tasks exploring a wide range of abilities, for example, memory, problem-solving and understanding. The tasks will involve a mixture of verbal responses and pen-and-paper exercises. It will take approximately 1 hour and 30 minutes in total, including at least one break in the middle.

After the assessment, we will arrange a follow-up appointment one week later where you will be asked to take part in some more short assessment tasks. The follow-up appointment will last a maximum of 30 minutes.

Expenses and Payments
You will be reimbursed for any public travel or petrol costs as a result of taking part in this research. Please talk to the researcher to arrange this.

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APPENDIX 13 (CONTINUED) - CONTROL GROUP INVITATION LETTER

What are the possible disadvantages and risks of taking part?
There are no known risks to taking part. If you feel tired at any time during the assessment, we can stop and/or take a break. Neither the questions nor procedures are in anyway harmful.

What are the possible benefits of taking part?
Your participation will contribute to help clinicians and epilepsy patients to better understand memory problems. The results of the study will also potentially assist further research in this area and the development of strategies for early detection and management of memory difficulties.

You can request to have a summary of the research findings. If you would like a summary then you will be asked to give some contact details so that we may send this to you.

What will happen to the results of the research study?
The results obtained from this research will be incorporated into a doctoral thesis that will be submitted to the University of East London. The thesis may be published in an academic journal, however any identifiable data about you will not be included in any report or publication.

Further Information:
Please feel free to ask the researcher any questions. If you are happy to continue you will be asked to sign a consent form prior to your participation. Please retain this invitation letter for reference.

What if there is a problem?
If you have any concerns about any aspect of this study, you should contact the Principal Investigator, who will do their best to answer your questions. If you remain unhappy and wish to complain formally, please contact the Research Supervisor [redacted] or the Chair of the School of Psychology Research Ethics Sub-committee.

Contact Details:

Principal Investigator:
[redacted]

Research Supervisor:
[redacted]

Chair of the School of Psychology Research Ethics Sub-committee
[redacted]

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APPENDIX 14 - LM EXTENDED DELAY ADMINISTRATION INSTRUCTIONS

19. Logical Memory Long-delay

19.1. Delayed Recall

Story B

SAY: *"Do you remember the stories I read to you last week? I want you to tell me the stories again. Tell me everything that you can remember about the first story. Start at the beginning."*

Record or score as the examinee recalls the story.

If the examinee does not recall any Story B details, SAY: *"The first story was about a woman who was robbed."*
Tick the **Story B Cue Given** box on the Record Form.
Do not give any further help other than general encouragement.

When the examinee has recalled as much of Story B as they can, proceed to Story C.

Story C

SAY: "*Now tell me everything that you can remember about the other story. Start at the beginning."*

Record or score as the examinee recalls the story.

If the examinee does not recall any Story C details, SAY: *"The second story was about a weather report."*
Tick the **Story C Cue Given** box on the Record Form.
Do not give any further help other than general encouragement.

When the examinee has recalled as much of Story C as they can, turn to Recognition for the Adult Battery.

19.2 Recognition

Recognition Story B

SAY: *"I am going to ask you some questions about the first story. Answer either yes or no. If you are unsure of your answer, just give your best guess."*

Read Story B questions in order from the record form.

Recognition Story C

SAY: *"I am going to ask you some questions about the second story. Answer either yes or no. If you are unsure of your answer, just give your best guess."*

Read Story C questions in order from the record form.

Scoring
- Circle N or Y. Correct responses are provided on the Record Form
- Questions may be repeated as often as necessary.
- Score 1 point per correct item

APPENDIX 15 - VR EXTENDED DELAY ADMINISTRATION INSTRUCTIONS

20. Visual Reproduction Long-delay

20.1. Delayed Recall

- Start point: Delayed Recall Item 1
- Discontinue: Do not discontinue

SAY: *"Last week, I showed you some pages with designs. I asked you to look at each design and then draw it for me. Do you remember?* [Ensure examinee remembers the VisRep designs task]. *Now, I want you to draw the designs again. You don't have to draw them in the same order as you did before. If one design was on a page, just draw one design. If two designs were on a page, draw both designs, just as you remember them. Let's begin. Draw any one of the designs here."*
[Point to response booklet]

Begin timing.

If the examinee says he or she does not recall the designs, provide general encouragement by saying,
"Each page had one or more designs on it" or *"Just try to remember any part of one of them."*

Do not prompt the examinee by describing in words a design or any part of a design or by drawing a fragment of the design for the examinee.

If the examinee attempts to reproduce other designs (e.g., designs from *Visual Puzzles*, symbols from *Coding*), SAY: *"I think this is one of the (patterns) (symbols) from a different test, where you had to (choose the parts that made up the design) (draw the symbol that went with the number). For this test I am asking you to remember the designs that I asked you to draw. They were made up of lines, in black and white."*

After the examinee completes each response, stop timing. Turn to the next page of the Response Booklet and SAY: *"Now draw another of the designs here."* [Point to response booklet]

Continue encouraging the examinee as necessary. Specific prompting is not permitted. Repeat these instructions until the examinee has drawn as many designs as he or she can remember. Remove the Response Booklet and pencils.

20.2. Recognition

Record: Circle the number corresponding to the examinees response for each item. Correct responses are provided on the Record Form.

SAY: *"Now, I am going to show you some more pages with designs. Each page has six designs. One of the designs matches a design you saw (and drew) last week. I want you to point to the design that matches the design you drew for me before. Ready?"*

Turn to recognition Item 1 in the Administration Manual.

APPENDIX 16 - VPA EXTENDED DELAY ADMINISTRATION INSTRUCTIONS

21. Verbal Paired Associates Long-delay

- Start point: Delayed Item recall 1
- Discontinue: Do not discontinue.
- Timing: Allow only 10 seconds for the examinee to respond to each item.
- During recognition – Say the words in each pair about 1 second apart.

21.1 Delayed Recall

Record incorrect responses verbatim.
SAY: *"Last week, I said some word pairs to you and asked you to remember the pairs. I repeated them, and asked you to tell me which word went with which. Now, I am going to say the first word of each pair that I said, and I want you to tell me the word that goes with it. Let's begin."*

SAY (for each item): *"Which word went with _____?"*

Read the first word of each pair in Delayed Recall in the order shown on the Record Form.
Allow 10 seconds for the examinee to respond.
Do not provide the examinee with feedback or the correct response.

If the examinee appears to be recalling sematically-related items (e.g., from the Similarities test),
SAY: *"I think that was one of the pairs from a different test, where you had to tell how the words were related, how they were alike or similar in some way. For this test I am asking you to say the word pairs that I asked you to remember. They weren't connected in any way."*

Turn to Recognition.

21.2. Recognition

- Record: Circle N or Y.
- Correct responses are provided on the Record Form.

SAY: *"Now I am going to say a word pair, and I want you to tell me if it is one of the pairs I asked you to remember last week. If it is one of the pairs I said before say "yes." If it is not, say, "no." Only say "yes" if both of the words in the pair match the word pair I said to you earlier. Ready?"*

If the examinee does not understand, you may repeat the directions, paraphrasing when necessary.
When you are sure the examinee understands the directions, start by reading Recognition Item 1.

Read each Recognition word pair in the order shown on the Record Form.

APPENDIX 17 - SUMMARY OF ANALYSED SCORES BY VARIABLE

	Variable	Analysed Score
Demographics	Age	Years
	Education	Years
	TOPF Estimated Premorbid Ability	Manual standardised score (M=100; SD=15)
Mood, sleep & subjective memory function	Everyday Memory Questionnaire (EMQ)	Raw score
	Hospital Anxiety and Depression Scale (HADS) - Anxiety	Raw score
	Hospital Anxiety and Depression Scale (HADS) - Depression	Raw score
	Pittsburgh Sleep Quality Index (PSQI)	Raw score
Non-memory cognitive functions	WAIS Similarities	Manual age-standardised score (M=10; SD=3)
	WAIS Visual Puzzles	Manual age-standardised score (M=10; SD=3)
	WAIS Digit Span	Manual age-standardised score (M=10; SD=3)
	WAIS Coding	Manual age-standardised score (M=10; SD=3)
	WMS Symbol Span	Manual age-standardised score (M=10; SD=3)
	WMS Spatial Addition	Manual age-standardised score (M=10; SD=3)
	DKEFS Letter Fluency	Manual age-standardised score (M=10; SD=3)
	DKEFS Category Fluency	Manual age-standardised score (M=10; SD=3)

APPENDIX 17 (CONTINUED) - SUMMARY OF ANALYSED SCORES BY VARIABLE

	Variable	Analysed Score
Non-memory cognitive functions (continued)	DKEFS Switch Total	Manual age-standardised score (M=10; SD=3)
	DKEFS Switch Accuracy	Manual age-standardised score (M=10; SD=3)
	Brixton Spatial Anticipation	Manual age-standardised score (M=10; SD=3)
Memory function	WMS Logical Memory Immediate Recall	Manual age-standardised score (M=10; SD=3)
	WMS Logical Memory Delayed Recall	Manual age-standardised score (M=10; SD=3)
	WMS Logical Memory Delayed Recognition	Ranked conversion (1-7) of manual aged cumulative percentile range (see Appendix 18)
	WMS Verbal Paired Associates Immediate Recall	Manual age-standardised score (M=10; SD=3)
	WMS Verbal Paired Associates Delayed Recall	Manual age-standardised score (M=10; SD=3)
	WMS Verbal Paired Associates Delayed Recognition	Ranked conversion (1-7) of manual aged cumulative percentile range (see Appendix 18)
	WMS Visual Reproduction Immediate Recall	Manual age-standardised score (M=10; SD=3)
	WMS Visual Reproduction Delayed Recall	Manual age-standardised score (M=10; SD=3)
	WMS Visual Reproduction Delayed Recognition	Ranked conversion (1-7) of manual aged cumulative percentile range (see Appendix 18)

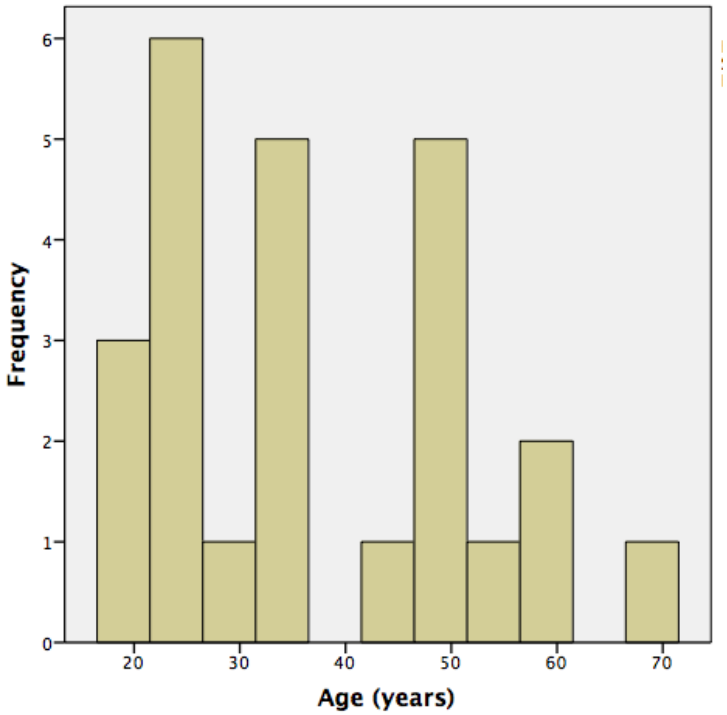
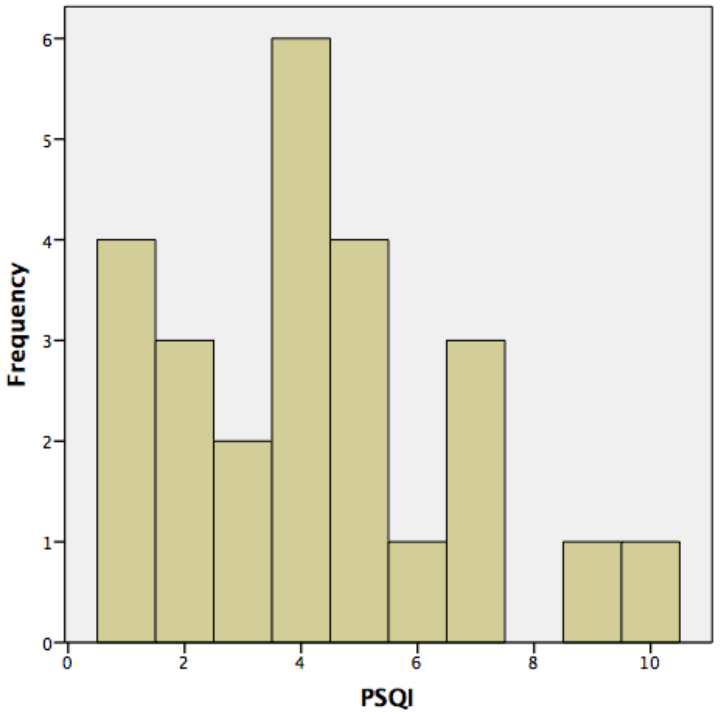
APPENDIX 17 (CONTINUED) - SUMMARY OF ANALYSED SCORES BY VARIABLE

	Variable	Analysed Score
Extended memory trials	WMS Logical Memory Extended Recall	Raw score
	WMS Logical Memory Extended Recognition	Raw score
	WMS Verbal Paired Associates Extended Recall	Raw score
	WMS Verbal Paired Associates Extended Recognition	Raw score
	WMS Visual Reproduction Extended Recall	Raw score
	WMS Visual Reproduction Extended Recognition	Raw score

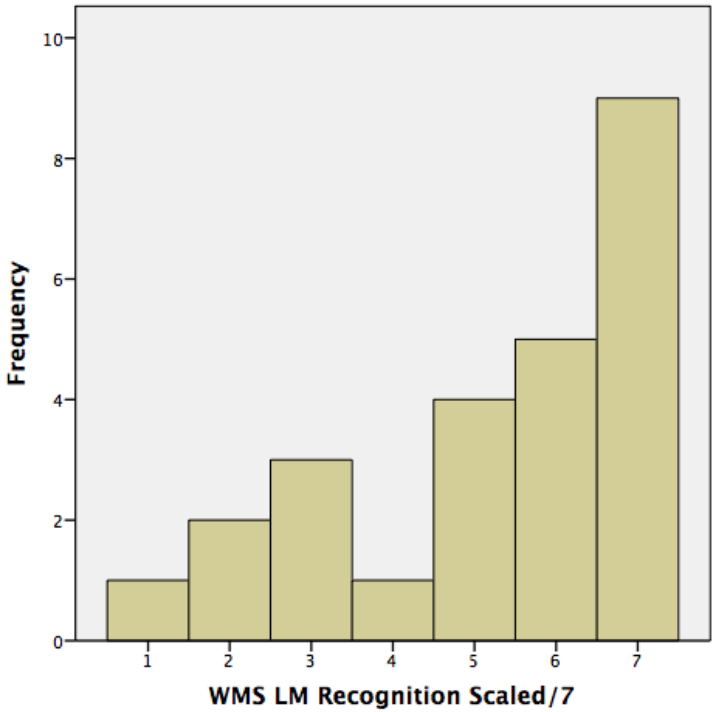
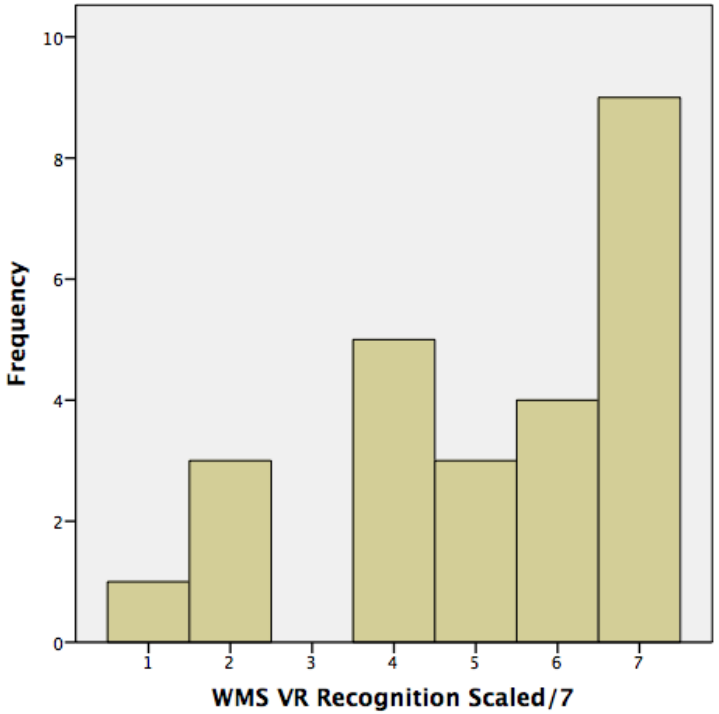
APPENDIX 18 - WMS RECOGNITION TASK SCORE CONVERSION FOR STATISTICAL ANALYSIS

Percentile Range	Ranked Score Conversion
>75	7
51-74	6
26-50	5
17-25	4
10-16	3
3-9	2
<2	1

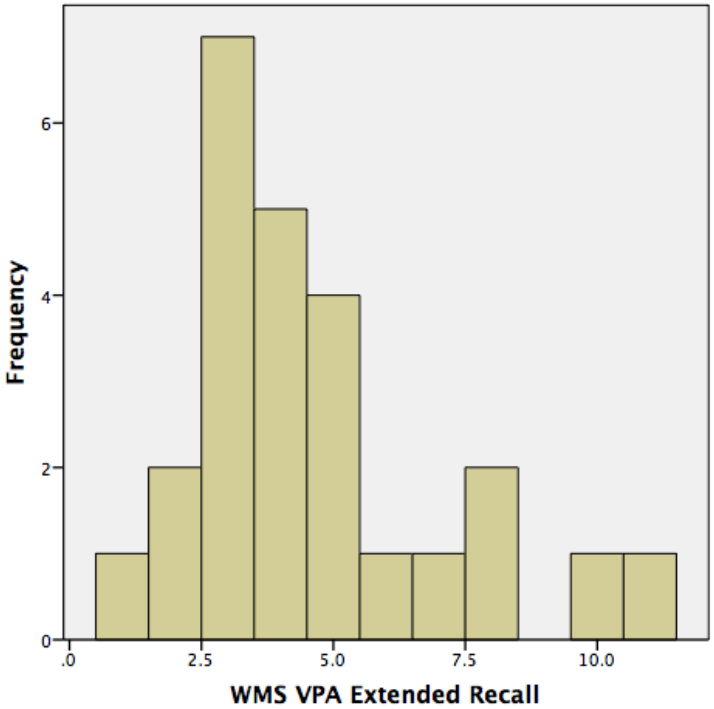
APPENDIX 19 - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Epilepsy Group	
Age (years)	PSQI (raw score)
	

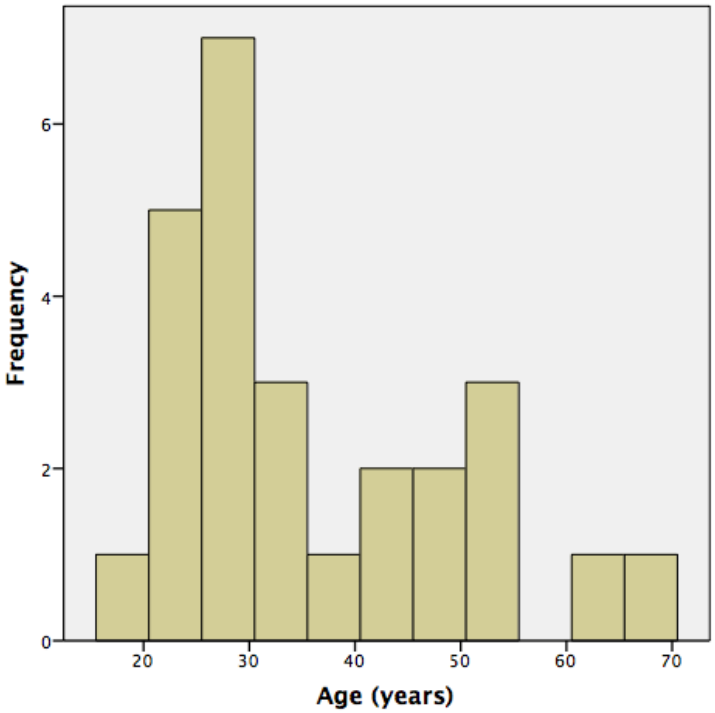
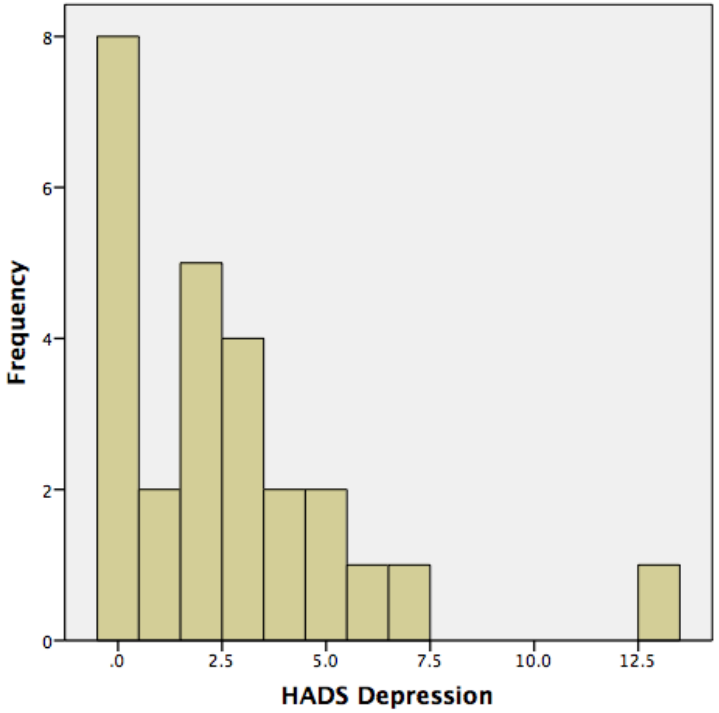
APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Epilepsy Group	
WMS Logical Memory Delayed (30-min) Recognition (scaled conversion)	WMS Visual Reproduction Delayed (30-min) Recognition (scaled conversion)
	

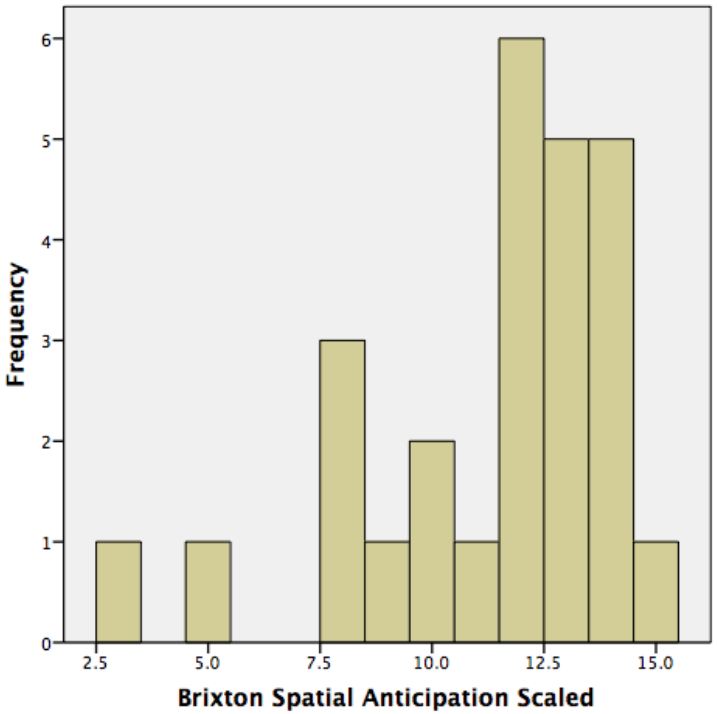
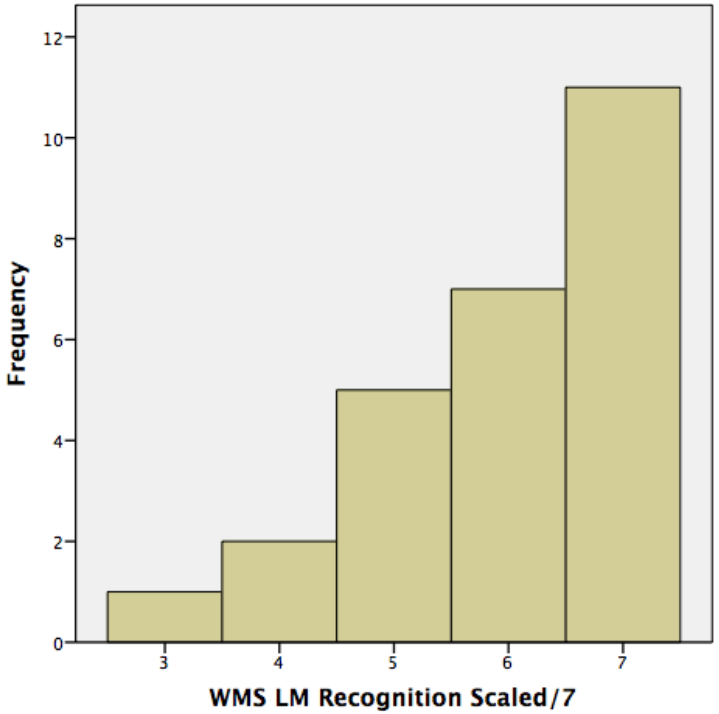
APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Epilepsy Group
WMS Verbal Paired Associates Extended (one-week) Recall (raw score)


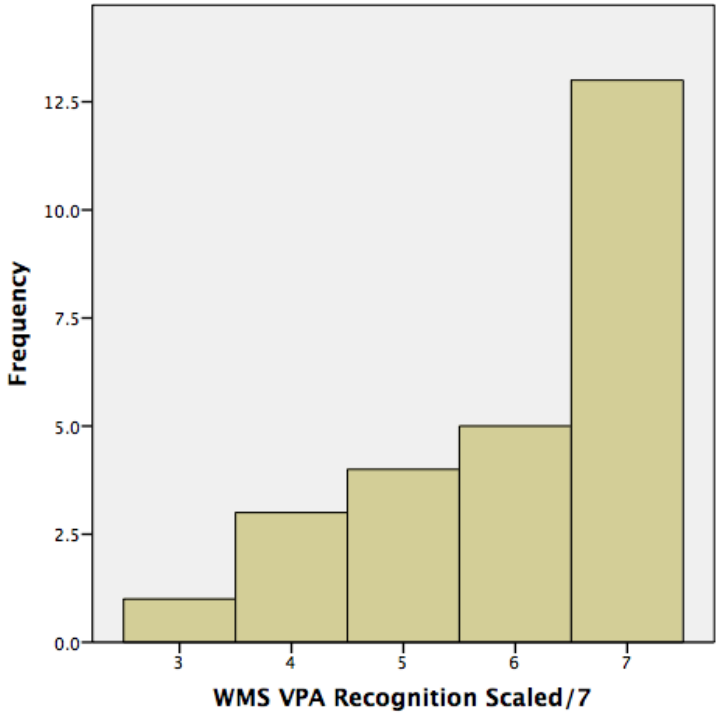
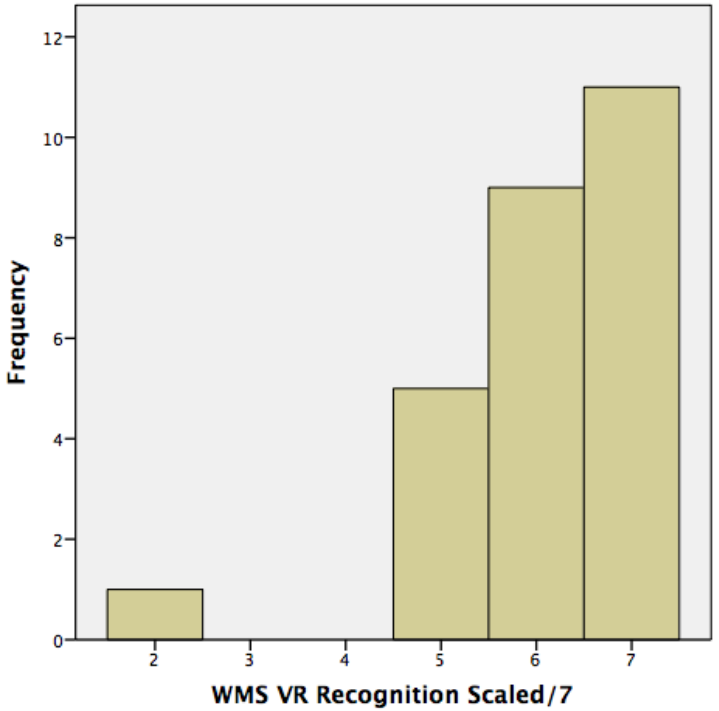
APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Control Group	
Age (years)	HADS Depression (raw score)
	

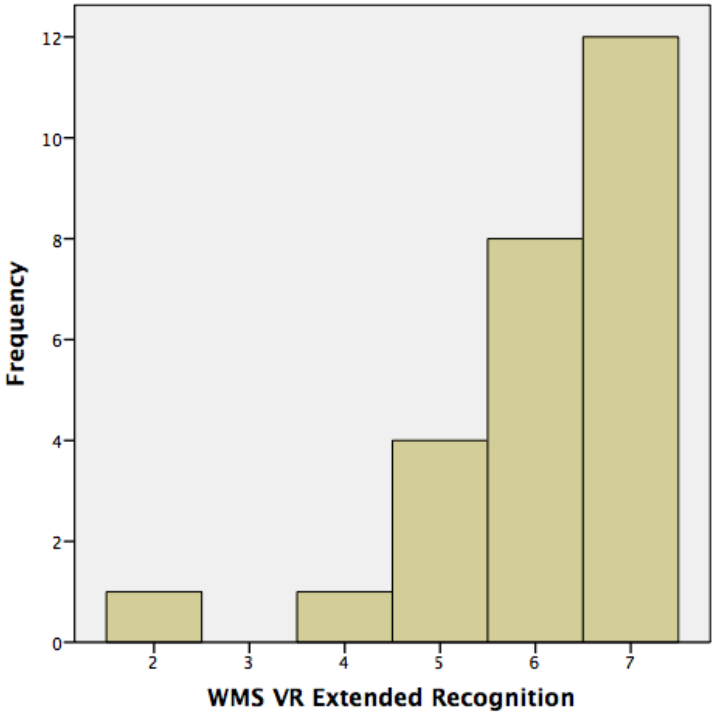
APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Control Group	
Brixton Spatial Anticipation (age-scaled score)	WMS Logical Memory Delayed (30-min) Recognition (scaled conversion)
	

APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Control Group	
WMS Verbal Paired Associates Delayed (30-min) Recognition (scaled conversion)	WMS Visual Reproduction Delayed (30-min) Recognition (scaled conversion)
	

APPENDIX 19 (CONTINUED) - HISTOGRAMS OF NON-NORMALLY DISTRIBUTED VARIABLES BY GROUP

Control Group
WMS Visual Reproduction Extended (one-week) Recognition (scaled conversion)


APPENDIX 20 - TITLE CHANGE FORM

APPLICATION TO CHANGE THE REGISTERED TITLE OF A THESIS FOR A POSTGRADUATE RESEARCH PROGRAMME

(TO BE COMPLETED BY THE DIRECTOR OF STUDIES AND THE STUDENT)

In completing this form you should refer to the relevant sections of the Research Degree Regulations (Part 9 of the UEL Manual of General Regulations) and the UEL Code of Practice for Postgraduate Research Programmes.

This form must be signed and dated in advance of submission to School Research Degrees Sub-Committee (SRDSC).

1. STUDENT'S DETAILS

FULL NAME	[redacted]	
UEL STUDENT NUMBER	[redacted]	
CURRENT MODE OF STUDY (DELETE AS APPROPRIATE)	**FULL-TIME**	~~**PART-TIME**~~
PROGRAMME FOR WHICH YOU ARE CURRENTLY ENROLLED *(Please Tick)*	**MPHIL**	
	MPHIL BY PUBLICATION	
	PHD VIA MPHIL	
	PHD DIRECT	
	PHD BY PUBLICATION	
	PROF DOC	**X**
	PHD (EUR)	
TITLE OF PROFESSIONAL DOCTORATE PROGRAMME (IF APPLICABLE)	**Professional Doctorate in Clinical Psychology**	
TITLE OF THESIS CURRENTLY REGISTERED	**Accelerated Long Term Forgetting in Temporal Lobe Epilepsy: The WMS-IV, Detection and Effects of Repetition**	
SCHOOL	**Psychology**	
NAME OF COLLABORATING ESTABLISHMENTS (IF ANY)	**NA**	

APPENDIX 20 (CONTINUED) - TITLE CHANGE FORM

2. PROPOSED CHANGE IN THE TITLE OF THE THESIS

PROPOSED NEW TITLE OF THESIS	**Investigating the Utility of the WMS-IV with Novel Procedures as an Assessment Tool for Accelerated Long Term Forgetting in Temporal Lobe Epilepsy**
REASON(S) FOR THE PROPOSED CHANGE	**Changes to analysis – original title no longer relevant to analysis conducted**

3. RECOMMENDATION OF THE SUPERVISORY TEAM

PLEASE NOTE THAT IN SIGNING BELOW THE DIRECTOR OF STUDIES INDICATES THAT THIS IS ON BEHALF OF, AND FOLLOWING CONSULTATION WITH, THE ENTIRE SUPERVISORY TEAM.
PLEASE NOTE THAT ELECTRONIC SIGNATURES ARE NOT ACCEPTABLE

WE RECOMMEND THAT THE CHANGE IN THE REGISTERED TITLE OF THE THESIS SHOULD BE APPROVED AS REQUESTED		
DIRECTOR OF STUDIES	**SIGNED:** [redacted]	
	PRINTED: [redacted]	**DATE: 02.04.15**

4. STUDENT'S CONFIRMATION

PLEASE NOTE THAT ELECTRONIC SIGNATURES ARE NOT ACCEPTABLE.

HAVING DISCUSSED THE PROPOSED CHANGE OF TITLE WITH MY SUPERVISORY TEAM, I AM SATISIFIED WITH THE PROPOSED CHANGE	
STUDENT	**SIGNED:** [redacted]
	DATE: 02.04.15