An exploration of semantic memory in the temporal lobe epilepsy population following unilateral resection

Sheeba Ehsan

Thesis submitted in partial fulfilment of the requirements of Staffordshire and Keele Universities for the jointly awarded degree of Doctorate in Clinical Psychology

May 2014

Acknowledgment Page

I am extremely thankful to my supervisors, Professor Matthew Lambon Ralph and Professor David Clark-Carter, whose encouragement, guidance and support enabled me to develop an understanding of a subject which is highly complex. I offer my thanks to all of those who supported me by providing vital input and patience during the completion of the thesis. A special thank you, to Dr Helena Priest and Dr Katherine Gerrard for proof reading the original papers. I am grateful for all the support my family provided. I especially thank my parents, Ehsan-ul Haq and Gulrez Anjuman, who have provided me with the moral support I required to complete this thesis. Finally, I would like to thank my friends whom have been extremely supportive in my endeavours.

Table of Contents

Thesis Abstract

Objectives: The aim of this thesis is to add to the knowledge base on semantic memory (SM) in temporal lobe epilepsy (TLE) following unilateral resection. **Method:** A systematically informed literature review was completed to identify existing literature. By reviewing the literature, a shortage of studies evaluating SM in this patient group was identified. It also highlighted disparity in objective measurement of SM. An under representation of subjective measurement via self-report was discovered, no apparent reason for this was identified. This literature review informed and provided the rationale behind a correlational study between objective and subjective assessment of SM. Using a case series methodology, SM was reviewed in a sample of 20 people with TLE who had undergone surgery. The aim was to compare self-reported SM difficulties with a standardised SM assessment. Self-report was also explored using content analysis to look at quality of life. **Results:** There was one significant finding with respect to self-report and neuropsychological tests, this was between self-reported problems with 'understanding conversations' and The 64-Naming Test, taken from the Cambridge Semantic Battery (Bozeat et al., 2000). Sensitive measures and sensitive questioning of SM were found to aid identification of changes in SM. In general, self-report ratings of memory were not significantly correlated with objective neuropsychological testing. Exploration of self-report data highlighted that an equal number of left (78%) and right TLE (73%) patients reported problems with SM. Five key themes were identified representing positive and negative factors post-surgery; emotional issues (65%) and adjustment issues (55%) predominated. Psychological issues seemed to reflect reports of depression more than anxiety. **Discussion:** Participants post-surgery were more sensitive to naming impairments than other forms of SM impairments. Self-report of naming impairments may indicate semantic processing difficulties, and therefore may be a valuable method to aid clinical assessment. **Conclusions:** Supplementing objective measurement with sensitive self-report assessment is useful in clinical practice.

Paper 1: A Systematic Review of Studies Investigating Semantic Memory Post Surgery for Unilateral Temporal Lobe Epilepsy

This review has been written for submission of publication to Neuropsychologia (see Appendix 1J for author guidelines) The journal was selected as the most appropriate means of disseminating the findings from this research as it attracts a broad audience.

Word count: 8687

KEY WORDS: Temporal lobe epilepsy, Surgery, Semantic Memory, Neuropsychological assessment.

Abstract

Semantic memory (SM) refers broadly to our knowledge about the world and other concept-based knowledge. Deficits in SM are widely regarded as one of the key defining features in semantic dementia, characterised by progressive aphasia and associated with bilateral atrophy of the anterior temporal lobes. Anterior temporal lobectomy is the standard treatment for medically refractory temporal lobe epilepsy (TLE). Deficits in episodic memory (EM) following surgery are well documented, whereas SM is often reported as intact. This is inconsistent with the theoretical standing of the role of the anterior temporal lobe in SM. It is of clinical importance to determine whether post-surgery SM difficulties do occur, as this aspect of memory plays a crucial role in everyday functioning. This paper aimed to review the literature regarding the effects of surgical intervention on SM in adults with intractable TLE. A secondary aim was to explore the use of subjective and objective measures to inform clinical practice. Searches were conducted on EBSCO Host, PsycINFO, Embase, MEDLINE, CINAHL, Web of Science, Clinical Evidence and The Cochrane Library. Twelve studies investigating SM in post-surgical resection TLE patients were identified. SM was assessed using various test materials and was not commonly reported as impaired. Possible reasons for this are discussed, including common representation of word finding difficulties and anomia which may mask SM impairments, resulting in under-representation of SM impairment. The studies in this review do not present a uniform picture and evidence for impairment is presented cautiously.

1.0 Introduction

1.1 Epilepsy

Epilepsy is a common neurological disorder, with an incidence of 2-5% and an estimated 50 million people worldwide being affected (World Health Organisation, 2001). The International League Against Epilepsy (ILAE) state that epilepsy refers to a group of conditions characterised by enduring seizures in the brain, with an epileptic seizure being defined as a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain (Fisher et al., 2005). It is not a single condition, with the All-Party Parliamentary Group on Epilepsy (2007) noting 30 different epileptic syndromes and over 38 different types of seizures. There are severe cognitive, psychological and social consequences of this condition (Fisher et al., 2000); including on the individual's education, employment, social life and mental health (Hermann & Jacoby, 2009). Temporal lobe epilepsy is a type of epilepsy which has a significant impact on cognitive, social and psychiatric functioning (Hermann, Seidenberg, & Jones, 2008). Lack of seizure control is debilitating for the individual and can significantly interfere with everyday functioning. Treatment usually consists of antiepileptic drugs (AEDs), however up to a third of individuals are resistant or refractory to AEDs (Schuele & Luders, 2008). For these individuals, epilepsy surgery can be an effective alternative (Engel et al., 2003). The aim of surgery is to remove the seizure generating region; the areas usually removed in an 'en bloc' resection are part of or all of the anterior temporal lobe of the affected side. Surgery has a good outcome, with 70% of patients becoming seizure-free and 95% reaching a reduction of seizure frequency of at least 90% (Engel, Cascino, & Shields, 1998, p.1687).

1.1.2 Temporal lobe epilepsy

Temporal lobe epilepsy (TLE) is a type of focal epilepsy which originates in the temporal lobes in the brain. It was defined in 1985 by the ILAE as a condition characterised by recurrent, unprovoked seizures originating from the medial or lateral temporal lobe (Commission on Classification and Terminology of the ILAE, 1989). AEDs are the preferred course of treatment; however seizure control is not achieved by AEDs in a third of patients with focal epilepsy (Kwan & Brodie, 2000).

The temporal lobes are common sites for the onset of seizures, and surgical resection of these areas is usually offered as a treatment option for refractory epilepsy (Ojemann & Valiante, 2006). Seizures in TLE usually originate from the mesial-basal temporal lobe structures, including the hippocampus, amygdala, and para hippocampal gyrus (Spencer & Burchiel, 2012). The hippocampal region is central to memory function (Eichenbaum, 2000).

Memory complaints are common in epilepsy; these are dependent on the laterality of the epileptic focus (Thompson, 1997, p.37), with left TLE causing more pronounced deficits in verbal EM, and, less consistently, right TLE affecting non-verbal memory (Hermann, Seidenberg, Schofield & Davies, 1997).

Surgery poses risks which require careful evaluation by the patient and the multi-disciplinary team (MDT). Prior to surgery, cognitive and behavioural out-comes are clinically assessed during the decision making process. Hippocampal sclerosis (neuronal cell loss and gliosis) in both left and right TLE patients has been associated with impaired aspects of semantic knowledge (Messas, Mansur & Castro, 2008). Post-surgical cognitive difficulties such as memory and language impairments pose the greatest risk, particularly verbal memory decline (Frisk & Milner 1990) and anomia (Bell, Davies, Hermann & Walters, 2000). Some studies report improvements in verbal memory and full scale IQ after resection of the non-dominant hemisphere (Hermann, Wyler & Somes, 1991). Other research suggests that no comprehension difficulties are present (Kho et al., 2008) and no generalised SM impairment exists (Simmons & Martin, 2009). Changes in language have not been reported consistently (Spencer & Huh, 2008).

1.2 Semantic memory and episodic memory

Over the past 20 years SM has received increased attention, facilitated by the rapid influx of imaging technology which enables mapping of behaviour and function. SM is a term coined and first documented in the title of Quillian's (1966) Ph.D. thesis, which led to a paper on the proposed structure of SM (Collins & Quillian 1969). SM was further distinguished from EM by Tulving (1972) and defined as a sub-system of long term memory. EM is defined as the memory store for personal events and the spatial relations in time amongst these, whereas SM is the memory necessary for the use of language (Tulving, 1972). SM represents 'organised knowledge that a person

possesses about words and other verbal symbols, one's concepts and relations' (Tulving, 1972, p.385). Examples (adapted from Tulving,1972, p.386) of individual memory statements for EM include 'I have an appointment tomorrow at 4pm to see my hygienist' and 'I was with friends when I heard the news of Princess Diana passing away'. As such, EM is closely linked to autobiographical events (times, places, associated emotions and other contextual knowledge) that can be retrieved and stated. In a memory test it may also encompass the knowledge required to remember the words presented in a list, and the order or pairing of words.

In contrast, examples of SM (adapted from Tulving,1972, p.386) include, for example, the knowledge that a) cats are furry animals, they have four legs and a tail; b) chairs can come in different shapes and sizes and are associated with tables; c) London is the capital city of the United Kingdom. All of these statements are subject to individual conceptual knowledge and depend upon the memory being acquired, but do not rely on personal experience in order to recall or use this information. Picture-picture matching tasks dependent on SM may require an individual to associate two objects such as a bottle of wine with a wine glass over a distractor item (champagne flute), or object naming, word-picture matching and the generation of exemplars on category fluency tests (e.g. animals, vegetables etc.) (Hodges,Patterson, Oxbury & Funnell, 1992). Overall, SM is the part of our long term memory which represents one's knowledge of objects, facts, and concepts and their inter-relationship (Tulving, 1972, 1983). The EM and SM systems have been described as distinct in function (Tulving, 1972); these findings have been advanced by clinical studies and the emergence of theoretical models of SM leading to anatomical insights (Shallice, 1988).

1.2.1 Neuropsychology of SM

SM is a critical factor in all aspects of everyday lives, therefore SM impairments can be highly debilitating. Neuropsychological evidence from disease processes that involve loss of SM facilitates an understanding of brain structures playing key features in SM. This can assist clinicians and researchers to have a greater understanding of clients and inform clinical interventions. Clinical psychologists, play a crucial role in the assessment of language and memory problems. In addition, working with epilepsy and other neurological conditions requires an understanding of the wider impact, for

example, on mental health, social, and societal factors. in order to provide appropriate support for the patient. There have been substantial advances in imaging technology which has led to a deeper understanding of the neural basis of SM and the causes of progressive disorders such as dementia. Dementia affects the brain, resulting in disturbance of multiple functions including memory (Scott & Barrett, 2007). The role of the clinical psychologist across neurologic populations includes, providing support to both the individual and their carers who may also struggle with the challenges posed by loss of memory and language abilities.

1.2.2 Theories of SM

Studies in the past led to the proposal that a structure-function relationship may exist in the brain, with specific areas of the brain being associated with particular functions (Galton, 1883). However, with advances in neuroscience, it has become easier to conclude that the brain is much more complex than this and that ascription of specific functions to discrete areas of the brain is flawed (Kanwisher, 2010). Although as a system many areas of the brain may be involved in processing of SM, there is growing evidence to suggest that the function of the anterior temporal lobe is significant. Over the years, many theories of SM have been proposed in efforts to encapsulate and understand its function. Whilst original theories suggested that SM arose from a central homogenous system in the brain with a distributed neural architecture (Fodor, 1983), these theories have been challenged by insights from neurological diseases which produce selective impairments, e.g. stroke (Berthier, 2001), herpes simplex virus encephalitis (HSVE) (Kapur et al., 1994), Alzheimer's disease (Giffard et al., 2001) and semantic dementia (SD) (Patterson, Nestor & Rogers, 2007). Evidence from degenerative brain disease has been associated with distinct patterns of neuropsychological deficit that correlate with the distribution of pathology (Neary et al., 1986).

Warrington (1975) first described selective SM impairment in three patients with semantic deficits across all modalities; however, limited neuroanatomical information was available. Perhaps the most striking evidence comes from neuropsychological studies of the neurodegenerative disorder of semantic dementia,

the temporal lobe variant of frontotemporal dementia (Snowden, Goulding & Neary, 1989). These patients present with relatively circumscribed progressive bilateral atrophy of the anterior temporal lobes, with correlating severity of atrophy in the inferior and lateral aspects of the anterior temporal lobe (ATL) (Nestor et al., 2006; Boxer, Rankin, & Miller 2003; Grossman, 2002; Mummery et al., 2000). On formal testing they fail on tests of SM across all modalities and concepts: receptive, expressive, verbal and non-verbal domains, with a striking preserved ability on other aspects of cognition and language, for example, perceptual and spatial skills, orientation, non-verbal problem solving, day to day memory, syntactic and phonological processing (Lambon Ralph, McClelland, Patterson, Galton & Hodges, 2001; Bozeat, Lambon Ralph, Patterson, Garrard & Hodges, 2000; Hodges et al., 1992). SD is progressive in nature and a typical presenting feature of patients is naming impairment (anomia), although comprehension difficulties can also be apparent (Lambon Ralph et al., 2001; Hodges, Graham & Patterson, 1995). As such, SD is highly debilitating, necessitating further exploration of its underlying mechanisms. Evidence from a range of SD patient studies using advanced techniques to assess the brain, for example magnetic resonance imaging (MRI), manual tracing methods and automated voxel-based morphometry (VBM) have shown atrophy of the temporal lobe (Williams, Nestor & Hodges, 2005; Mummary et al., 2000). Evidence from post mortem studies of SD patients has found widespread volume loss relative to controls, with ATL regions most affected (Davies, Halliday, Xuereb,Krill & Hodges , 2009). These findings suggest that SM is implicated in the ATL, and that the breakdown in knowledge is linked to ATL damage thus leading to dysfunction.

1.2.3 Role of the anterior temporal lobe in SM

Many theoretical models have been proposed to assist an understanding of the role of the ATL in SM. Relevant evidence comes from studies investigating semantically impaired patients, which also provide details on locus of their brain lesions. As such, studies of SD patients show impairment independent of task and are consistent across modalities (Bozeat et al., 2000), leading to the theory of a single store of amodal semantic knowledge or a semantic ‘hub’ (Rogers et al., 2004). The

semantic ‘hub’ theory has been replicated in studies utilising computational parallel-processing models (Rogers et al., 2004). There is growing evidence for the role of the ATL encompassing the semantic hub, which is central in semantic cognition (Patterson et al., 2007). The amodal model enables an understanding of a complex system that is known to receive input from many modalities, e.g. sensory, motor and language, and is able to generalise across concepts that have similar semantic significance, for example, two items may appear dissimilar but belong to the same category (Patterson et al., 2007). Damage to this area should result in a gradual decline in SM as evident in SD (Rogers et al., 2004; Lambon Ralph & Patterson, 2008). Another theory proposed by Damasio et al., (2004) suggests a similar function for specific brain regions acting as “convergence zones” to bring together sensory and motor output. The temporal lobe has connections with the prefrontal cortex and the three temporal gyri which receive input from the crucial areas of the brain, for example, the ventral visual processing stream, somatosensory, visual and auditory processing streams and speech perception areas, assumed as ideal for amodal semantic representations (Rogers et al., 2004; Patterson et al., 2007).

Converging evidence for the role of the ATL in SM has also been provided in healthy participants using transcranial magnetic stimulation (TMS) of the lateral anterior temporal lobe (Pobric, Lambon Ralph & Jefferies, 2007). In addition, evidence from imaging studies mainly using positron emission tractography (PET) and tasks involving semantic processing have shown significant left ATL activation (Mummery, Patterson, Wise, Price & Hodges, 1999) or bilateral activation (Rogers et al., 2006) in healthy participants.

The role of the ATL in SM is clearly supported by the above patient and non-patient groups. Unilateral temporal lobe epilepsy (TLE) is another condition which may contribute to the understanding of the function of the ATL in SM. A review of the existing evidence in TLE and SM to determine whether it is consistent with the evidence discussed above would therefore be beneficial.

This investigation aims to systematically review the existing literature regarding TLE and SM; a review of existing literature shows that this does not appear to have

been previously carried out (Appendix 1J). If SM is located in the ATL, removal of this area should provide further insights into the role of the ATL.

2.0 Aims

The aim of this review is to assess the effects of surgical intervention on SM in adults with intractable TLE. A secondary aim is to explore the use of subjective and objective measures to inform clinical practice.

3.0 Design

The literature was systematically reviewed according to guidelines published by the Cochrane Collaboration (2011). In order to achieve as comprehensive a search as possible, searches of several electronic databases were conducted as recommended by Whiting (2008).

4.0 Method

4.1 Search strategy

Relevant studies were identified by a comprehensive, systematic search of electronic databases EBSCO Host, PsycINFO, Embase, MEDLINE, CINAHL, Web of Science, Clinical Evidence and The Cochrane Library. Information was obtained on the subject terms using the information function in the database. This provided date of inception, e.g. Database: PsycInfo, term: epilepsy, date: 1967 to May 2012. This date was utilised in the search criteria. The review used a subject search strategy with *temporal lobe epilepsies* and *semantic memory* as the main search terms. The main subject headings were exploded to include terms that mapped onto the search strategy, e.g. epilepsy or temporal lobe epilepsy; semantic memory or memory or semantics (Appendix 1A). Keywords were searched in all fields: *surgery* was searched separately then a search for the terms *operation* OR *lobectomy* OR *resection* OR *excision* was conducted using truncation. Once the search string was built these results were combined (Appendix 1B). Further to a complete search of all the databases (Appendix 1C), the results were combined using the bibliographic software RefWorks and duplicates were eliminated (Appendix 1D).

4.1.1 Inclusion/Exclusion criteria

Titles and abstracts were screened and studies were included if they met a number of criteria (see below). Studies were not excluded on the basis of methodology; however studies utilising quantitative methodology were the main focus.

The inclusion criteria were as follows:

(1) Published in English.

(2) Adult participants with a diagnosis of unilateral TLE who had undergone surgery for seizures refractory to antiepileptic drug treatment.

(3) Presentation of original data including neuropsychological reports for this sample pre and or post-surgery.

(4) The neuropsychological battery included a measure of SM and clearly stated this.

(5) The paper presented psychometric findings and exploration of the relationship between TLE and SM post-surgery.

The exclusion criteria were as follows:

(1) Studies involving child participants, as epilepsy surgery in children has additional complicating factors including differing age groups, unique surgical considerations, detrimental effects of seizures on the developing brain, the capacity for functional plasticity in younger brains, memory and, develop- mental stages (Spencer & Huh, 2008).

(2) Studies not employing standard en bloc resection.

(3) Studies of late onset epilepsy secondary to other factors, for example, brain injury.

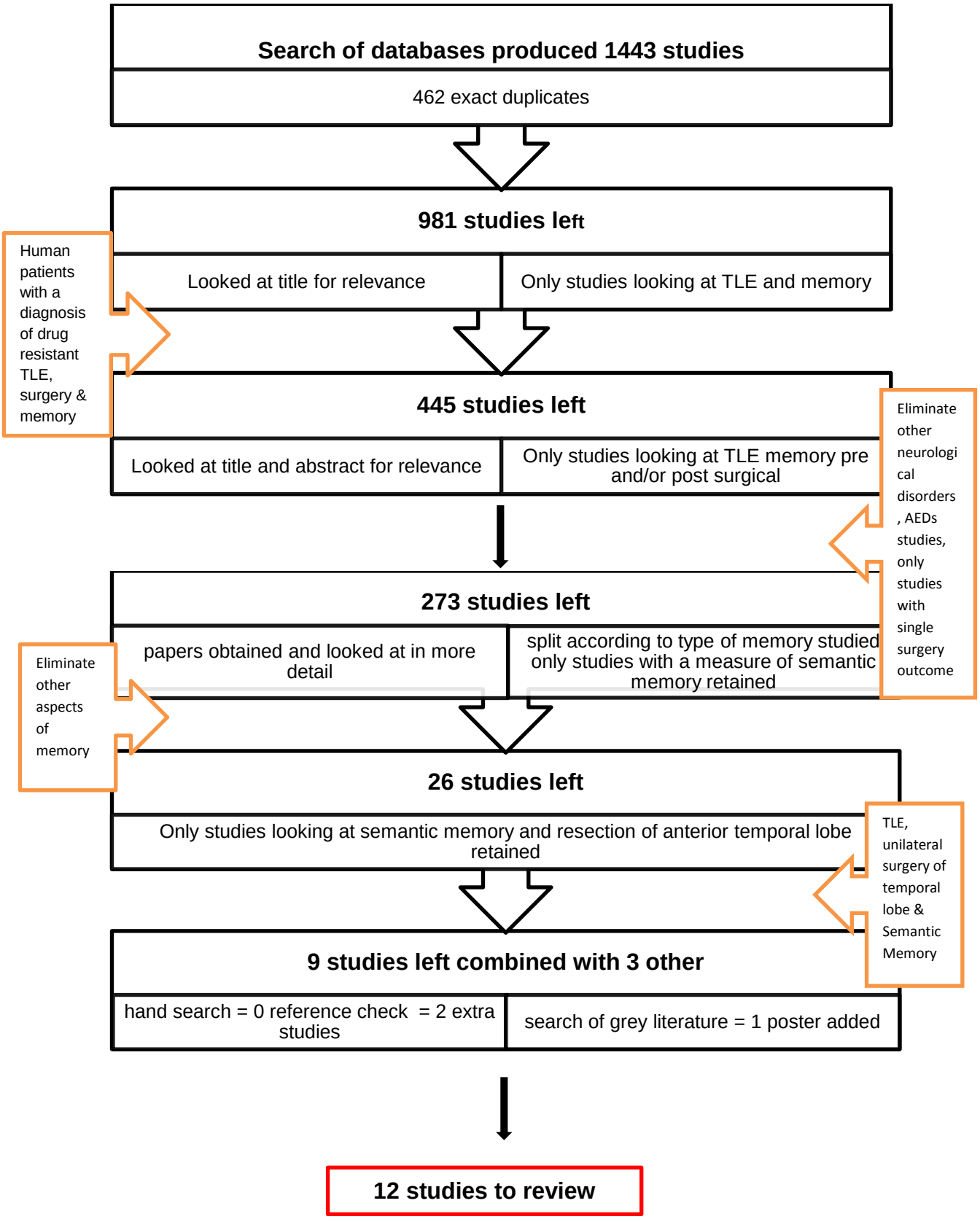
The research to date in this area remains sparse; therefore any study that mentioned semantics and temporal lobe epilepsy was obtained. No studies exploring SM and surgery from a qualitative perspective were identified by the search.

4.2 Search outcome

The search strategy produced 1,443 papers (Appendix 1C). A hand search of *Epilepsy and Behaviour* and *Epilepsia* was carried out from April 2012 to Feb 2005 to identify publications that may not have been identified during the search. A Google search was conducted to identify unpublished literature, which identified one poster which was included. The initial search output was screened by the author and 50% was screened by the academic supervisor. Agreement on studies to include/exclude was arrived at through discussion.

The papers were filtered as shown in Figure 1 (see Appendix 1H). Twelve studies were reviewed

4.2.2. Figure 1: Flow diagram of search outcome



4.3 Characteristics of included publications

In relation to study design, the twelve studies selected consisted of eight pre - and -post-surgery assessments (Martin, Loring, Meador & Lee,1990; Hermann, Wyler, Somes, Dohan & Clement, 1994; Hermann, Seidenberg, Haltiner & Wyler, 1995; Martin et al., 1998; Drane et al., 2008; Koylu, Walser, Ischebeck, Ortler & Benke, 2008; Schwarz & Pauli, 2009; Kim et al., 2010), two case series designs (Wilkins & Moscovitch, 1978; Lambon Ralph, Ehsan, Baker & Rogers, 2012), one cross sectional study (Schmolck et al., 2005) and one single case study (Ellis, Young & Critchley, 1989). All studies reported using neuropsychological measures; some measures were reported to be specifically selected for that study whilst others were part of a screening battery for surgery. There was a small overlap between the tests employed. One study used subjective questionnaires (Ellis et al., 1989). Two studies reported using measures in another language (see table 3) (Koylu et al., 2008; Kim et al., 2010). Participants were reported as having TLE, anterior temporal lobectomy (ATL), or medial TLE with or without hippocampal sclerosis. All studies reported patients undergoing standard resection (ATL) or selective amygdalo-hippocampectomy (SAH) (Appendix 1G). Four studies stated exploration of SM as a main aim (see table 3). Three reported exploring semantics as connected to language, e.g. fluency. One explored the effects of hippocampal sclerosis and surgery on different aspects of memory; three studies looked at solely verbal or verbal and visual memory, and one explored general memory change post-surgery.

4.4 Quality assessment

The term methodological quality is often used to refer to “internal validity” which is the extent to which a study is free from major methodological biases (Petticrew & Roberts, 2006). The quality of studies was assessed using a 15-item checklist devised by the author (Appendix 1E). The checklist was based on the premise that the studies mainly represented case control studies and they were quantitative in nature. The Critical Appraisal Skills Programme (CASP) tool (Public Health Resource Unit, 2006) for case studies was explored using guidelines

derived from a number of sources (Greenhalgh 2001; Kitchenham 2004) on developing quality instruments. Checklists are usually based on attention to factors that could bias study results, including both generic and specific items. For each item, a study received a score of one if the criterion was met and a score of zero if it was not. A rating of 'not applicable' was given if the question was not appropriate for that study.

The quality assessment was completed independently by the author and by the academic supervisor. Further to this, scores were compared and a consensus was reached where disagreements arose.

4.4.1 Data extraction

Data extraction sheets were used to highlight key aspects of each study (see Appendix 1F). The following information was extracted and recorded from each paper: title; author(s); year of publication; study objectives; design; measures of memory used; sample size and key findings.

4.4.2 Quality appraisal

As research into the area of SM and TLE is still in its infancy, all studies explicitly testing for semantics, including semantic fluency, were included. Table 1 shows that all of the studies clearly defined their target population, defined their objectives, used an appropriate design to address the study question, defined their outcomes, used subjective/objective measures across all their participants, used an appropriate analysis and gave a description of this, and addressed limitations where appropriate.

4.4.3 Data synthesis

A systematic review and synthesis of the research findings is provided to help summarise and identify key strengths and limitations from the included studies. This method was considered most appropriate given that there was

limited data that could be pooled because of heterogeneity in study designs and outcome measures.

4.4.4 Synthesis of results

(Please refer to Table 1 and Table 2)

The studies scored between 9-14 out of a possible 14 or 15 on the quality checklist. The samples were primarily from epilepsy clinics; eight studies provided details on the selection process of participants. All of the studies defined the target population, but none provided details of the power analysis used to determine sample sizes and therefore it is not possible to comment on this aspect. All studies provided clear objectives and a rationale for their study design choice. All the studies addressed the study question and used subjective or objective measures (see Table 2). Only two studies made any reference to the reliability or validity of the tests used (Drane et al., 2008; Lambon Ralph et al., 2012); the measurements were used across groups as appropriate. Seven studies used a control group (Wilkins & Moscovitch, 1978; Ellis et al., 1989; Martin et al., 1990; Drane et al., 2008; Kim et al., 2010; Lambon Ralph et al., 2012; Schmolck et al., 2005). Two of the studies did not make any explicit reference to possible confounding factors (Wilkins & Moscovitch, 1978; Schmolck et al., 2005). Only one study (Koylu et al., 2008) included a follow up design. The analysis was described appropriately for all the studies. All studies addressed study limitations except one (Wilkins & Moscovitch, 1978).

For the purpose of this review, attention was paid to the following: sample size, interval between surgery and post-operative testing, measures used to assess semantic memory, semantic memory outcome, findings in line with the current literature, and predictive factors (see Appendix I).

The sample size of the studies ranged from 1-101 (mean = 42, SD = 32). The single case-study (Ellis et al., 1989) reported a right temporal lobectomy patient, with no selection justification.

All patients were split according to right or left seizure onset (See Appendix I). Eight studies employed a pre and post study design; time to post-surgical re-

test varied with one study re-testing one week after surgery (Martin et al., 1990). The impact of testing at the acute stage of resection was discussed and justification offered by the authors. The acute stress of surgery and anaesthesia on cognitive performance is well documented (Hanning, 2005); a gap of at least one year is reported as ideal (Hermann et al., 1999). Three studies reported testing at six months post-surgery (Hermann et al., 1994; Hermann et al., 1995; Schwarz & Pauli, 2009), two studies reported testing up to 12 months after surgery (Martin et al., 1998; Koylu et al., 2008) and two reported testing at one year post surgery (Drane et al., 2008; Kim et al., 2010). In one of the studies (Ellis et al., 1989), a single patient was tested 14 years post-surgery with no pre surgical testing reports. Wilkins and Moscovitch (1978) tested between one and 21 years post-surgery. Post-surgical testing was reported at least one year later in the remaining studies (Lambon Ralph et al., 2012; Schmolck et al., 2005) with no pre surgical testing reports. Two of the studies consisted of data, which was in-part from the same sample (Hermann et al., 1994; Hermann et al., 1995).

4.4.5. Table 1. Checklist results: Quality of studies

Criteria	Wilkins & Moskovitch (1978)	Ellis et al(1989)	Martin et al (1990)	Hermann et al (1994	Hermann et al (1995)	Martin et al (1998)	Drane et al. (2008)	Koylu et al (2008)	Schwarz & Pauli (2009)	Kim et al(2010)	Lambon Ralph et al (2012)	Schmolck et al (2005)
Is the population clearly defined?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Is the selection process of participants described?	×	×	×	✓	✓	✓	✓	✓	✓	✓	×	✓
Are the objectives of the study defined?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Is the design appropriate?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Did it address the study question?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Are the outcomes clearly defined?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Did they use subjective or objective measurement?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Justification of validity/reliability of measures?	×	×	×	×	×	×	✓	×	×	×	✓	×
Are the measurement methods similar across groups?	✓	N/A	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Was a control group used?	✓	✓	✓	×	×	×	✓	×	×	✓	✓	✓

Have the authors identified possible confounding factors in the sample or design?	×	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	
Was there a follow-up?	N/A	×	×	×	×	×	×	✓	N/A	N/A	N/A	N/A	
Is the analysis described?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Is the analysis appropriate?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Are any limitations of the study addressed?	×	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Percentage of maximum quality of score	**10/14 71%**	**11 /14 78.5%**	**12 /15 80%**	**12/15 80%**	**12/15 80%**	**12/15 80%**	**14/15 93%**	**13/15 86.6%**	**12/14 85.7%**	**13/14 93%**	**13/14 93%**	**12/14 85.7%**	**Mean 84%**
Marks lost	**4**	**3**	**3**	**3**	**3**	**3**	**1**	**2**	**2**	**1**	**1**	**4**	**Mean 2.5**

✓Present; × absent; N/A, not appropriate.

4.4.6 Subjective and objective measures

(Please refer to Table 2)

The 12 studies utilised various standardised neuropsychological tests, to measure different aspects of memory including SM. The number used ranged from three to 13 and consisted of pre-surgical and post-surgical assessments. Eight studies reported pre surgical assessment data (Martin et al 1990, 1998; Hermann et al, 1994, 1995; Drane et al., 2008; Koylu et al., 2008; Schwarz & Pauli, 2009; Kim et al., 2010); four studies reported IQ scores using a version of the Wechsler Adult Intelligence Scale (WAIS or WAIS revised; Wechsler 1981, 2008) (Ellis et al, 1989; Hermann et al, 1994; 1995; Martin et al, 1998). One study reported using the German multiple choice vocabulary intelligence tests (Mehrfachwahl Wortschatz-Intelligenz test) (Schwarz & Pauli, 2009); for the three remaining studies it was not possible to ascertain which measures of IQ were employed. One study reported post surgically on IQ utilising the WAIS (Wilkins & Moskovitch, 1978). The findings of the studies reported depended on a number of validated measures to assess SM and other aspects of memory.

4.4.7. Table 2. Overall methodology and results summary for twelve articles on SM

Study	Participants	Objectives	n	Design	Measures	Results/conclusion
Wilkins & Moscovitch, (1978)	TLE	SM impairment after temporal lobectomy	22	Case-series	Wechsler-Bellevue intelligence, cued-naming, Living/man-made drawings, un-cued naming, larger/smaller drawings, living, man- made words, larger/smaller words	Left impaired at naming un-cued drawings, also classifying as living or man-made. Selective impairment in SM
Ellis *et al.*(1989)	TLE	Explore memory impairment further to surgery	1	Case study	WAIS, WMS, NART, Rey figure, faces line-up test, names line-up test, Famous voices test, The Famous personalities test, Dead-or-Alive test, Object naming, Category membership decisions for living & non-living , Famous animals, Famous buildings, monuments, old product names, QA	Loss of biographical knowledge. No generalised SM deficits for living things
Martin *et al.* (1990)	TLE	Testing word fluency in TLE both formal and semantic	32	Pre/Post	Controlled oral word association test (MAE) & Semantic fluency task, IQ	Language dominant resection associated with postsurgical language deficit
Hermann *et al.*(1994)	TLE	Testing word fluency in TLE both formal and semantic	62	Pre/Post	WAIS-R, CVLT, MAE FRT, Line Orientation, Snellen eye chart	No effect of hippocampal pathology on immediate or SM. No SM impairment.
Hermann *et al.* (1995)	TLE	Age at onset, chronological age and pre and post verbal memory	101	Pre/Post	WAIS-R, CVLT, WMS, MAE (visual naming)	Left ATL decrease in EM indices but not on SM
Martin *et al.* (1998)	ATL	Characterise patterns of base rate change on	101	Pre/Post	WMS (logical memory, visual reproduction) WAIS-R, CVLT,BNT	Decline in verbal semantic & episodic memory tasks in left ATL,

		measures of verbal & visual memory after ATL				decline in immediate & delayed episodic in right ATL
Drane *et al.* (2008)	ATL	Category-specific naming and recognition deficits	22	Pre/Post	BNT, Category-specific famous faces, animals, objects, naming, recognition, MAE, Fluency, FRT, Line Judgement	Category-specific naming and recognition deficits in ATL, missed by BNT. No general SM impairment. Anomia may reflect SM problems
Koylu *et al.* (2008)	TLE	Relationship between MTL activation and verbal memory performance	26	Pre/Post	IQ, CVLT (German version), Adapted version-Semantic decision & tone decision task (Binder et al, 1997), fMRI	Correlations between MTL activation and both preoperative and postoperative verbal memory. Lateralisation of SM
Schwarz & Pauli (2009)	TLE	Functional relationship between post - operative object naming & semantic phonological speech	58	Pre/Post	BNT, Auditory & visual speech comprehension test for word meaning, Auditory comprehension test for words, Word production test, Verbal intelligence (Mehrfachwahl-Wortschatz-Intelligenztest)	Naming decline post-surgery in left TLE, association between post-operative naming decline & impaired semantic functions
Kim *et al.* (2010)	mTLE with HS	Brain plasticity associated with semantic aspects of language function	19	Pre/Post	Language tasks (Korean); sentence reading, pseudo-word reading, word generation, fMRI	No difference was noticed in activations pre surgery. Surgery did not alter the phonological-associated activations. Reorganisation of SM network
Lambon	TLE	Test SM directly in	20	Case-	Camden Recognition memory Battery	Evidence of semantic

Ralph *et al.* (2012)		TLE following surgery		series	(words/faces), digit span (forward/backwards), Rey Figure, Raven's coloured progressive matrices, Cambridge Semantic Battery 64 picture naming, Object action-to-picture matching task, word-picture matching, GNT, GFT, 96 Synonym judgement, Number-decision task	memory impairment
Schmolck *et al.* (2005)	TLE(Pre/Post)	Compare SM in left & right TLE & the impact of surgery	40	Cross-sectional study	Naming to picture, naming to definition, definition to picture, IQ	Naming to picture impacted by surgery in dominant ATL, pre and post ATL difficulty with definition task

Temporal Lobe Epilepsy (TLE); SM (SM); Anterior Temporal Lobe (ATL); Medial Temporal Lobe (MTL); Medial Temporal Lobe Epilepsy (mTLE); Hippocampal Sclerosis (HS); Episodic Memory (EM); California Verbal Learning Test (CVLT); Wechsler Adult Intelligence Scale (WAIS; WAIS-R is revised); Wechsler Memory Scale (WMS); Boston Naming Test (BNT); Graded Naming Test (GNT); Graded Faces Test (GFT); National Adult Reading test (NART); Facial Recognition Test (FRT); Multilingual Aphasia Examination (MAE); Questionnaire (QA)

4.4.8 Memory & language outcome

Two studies reported no change in SM following surgery (Herman et al., 1994, 1995). Two studies utilising fMRI reported change but in the semantic language network, indicative of compensation or functional recovery and reorganisation following surgery (Koylu et al., 2008; Kim et al., 2010). Schmolck et al. (2005) reported findings on SM as incomplete; however, they suggest that patients' ability on SM tasks decreased further to dominant ATL resection. Five of the studies provided some indication of SM impairment. Martin et al. (1990) reported that formal and semantic based word fluency performance was affected regardless of language laterality; language dominant resection is associated with postsurgical language decrease. Martin et al. (1998) reported no change in SM in the right resected TLE group, but found a decrease in the left resected group. Three studies found category specific deficits including category differentiation of semantically related objects (Schwarz & Pauli, 2009), and category specific deficits for naming animals and famous faces (Drane et al., 2008) implicating SM decrease.

One study concluded that their participant had generally good memory and did not have generalised SM impairment, but this was decreased when retrieving specific knowledge, for example, regarding famous people and famous animals (Ellis et al., 1989). The authors were inconclusive regarding the nature of the deficit between a semantic store impairment versus impaired access to the store itself, concluding that their participant had suffered damage to the SM system with the synthesis of episodic and autobiographical memories. The authors also used two subjective questionnaires that showed good agreement with the formal test results. Significant decrease in SM post-surgery was reported by two studies. Wilkins and Moskovitch (1978) found that patients who underwent left temporal lobe resection exhibited selective SM decrease involving the classification of figures and names, and Lambon Ralph et al. (2012) reported that all participants had decreased SM compared with performance on non-semantic tasks. Overall the studies in this review utilise different measures and are not comparable due to heterogeneity.

The studies reported in this review are generally consistent with the existing literature regarding the outcome of surgery in TLE, which report naming deficits (Wilkins & Moskovitch 1978; Martin et al., 1998; Drane et al., 2008; Schwarz & Pauli, 2009; Lambon Ralph et al., 2012; Schmolck et al., 2005). Perhaps naming impairments are generally more consistently assessed rather than SM. It has also been suggested that naming impairments are probably more prevalent and often missed by standard clinical measures, and that classic anomia seen post-surgically in TLE may in fact disguise SM problems (Drane et al., 2008). Speech production requires both knowledge of the meaning of words and phonology, and anomia may reflect damage to the underlying semantic system (Lambon Ralph, Sage, Roberts, 2000). Therefore, further clinical exploration is required to investigate the cause of anomia, i.e. whether this is due to an underlying access problem rather than storage. Two studies described reorganisation of memory function as a result of surgery; semantic activations became more bilateral in left TLE and more left lateralised in right TLE (Kim et al., 2010). In the other study, SM processing caused bilateral activations in both left and right TLE (Koylu et al., 2008). These studies provide evidence for brain plasticity and perhaps functional recovery of memory.

4.4.9 Predictive factors

Of the 12 studies reviewed, five researched predictive factors of memory decline. Martin et al. (1990) measured blood levels of antiepileptic medication and reported no significant difference post-surgery. Herman et al. (1994) carried out detailed analysis of hippocampal sclerosis and concluded that no/mild hippocampal sclerosis was a predictor for post-operative EM decline mainly in left TLE. Another study found that factors such as later age of onset of epilepsy and older chronological age at time of surgery were significant predictors of EM decline in left TLE (Herman et al., 1995). One study (Martin et al., 1998) utilised regression based methodology to look at the predictive utility of baseline memory measures on postoperative memory outcome. The authors reported that individual prediction from group-level analyses is difficult as it may disguise individual outcomes by combining the proportion of patients who improved, declined, and

showed no change post-surgically. Koylu et al. (2008) reported correlations between medial temporal lobe activation and both pre and post-operative verbal memory, finding that activation in the right medial temporal lobe of left TLE patients was predictive of better memory outcome post-surgically.

5.0 Discussion

This review aimed to assess the effects of surgical intervention on SM in adults with TLE. Another aim was to explore the use of standardised and self-report measures to inform clinical practice. In this review, SM impairments were not frequently reported. Eight studies provide evidence for a role of the temporal lobe in SM functions (Wilkins & Moscovitch 1978; Ellis et al., 1989; Martin et al., 1990; 1998; Koylu et al., 2008; Schwarz & Pauli, 2009; Kim et al., 2010; Lambon Ralph et al., 2012); however, only two studies reported decline in SM across measures (Wilkins & Mocovitch, 1978; Lambon Ralph et al., 2012). While these findings are difficult to reconcile due to the heterogeneity of the studies sampled, few studies have been undertaken to directly assess the question of SM impairment in post-surgical TLE. The studies that have directly looked at this aspect have probed SM using a variety of tests. Overall, 12 studies were included and the quality of the studies reviewed was found to be good. Whilst reviewing the studies it became apparent that a huge disparity exists in the literature between design and methodology including sample size and measures of SM.

The studies reviewed did not provide justification for the sample sizes and no power calculations were provided, therefore limiting generalizability. Real world research presents the challenge of recruiting from discrete populations, limiting how many people may be recruited over a short period of time, a limitation that was not acknowledged by the studies in this review. A variety of methodologies were used, with pre/post-surgery designs allowing greater control to discern whether any change is due to the surgery versus the impact of epilepsy. Evidence from other brain surgery populations suggests a certain amount of recovery ensuing brain surgery indicative of plasticity (Daffau et al., 2003); highlighting implications for testing soon after surgery.

The measures used to evaluate SM are diverse and only one of the studies used self-report measures (Ellis et al., 1989). Memory problems are generally part of the epilepsy sequelae and epilepsy surgery is a highly invasive procedure. Bridging the gap between day-to-day memory problems and those reported on objective measures and a measure of self-report could be crucial. Especially as our memories define us, and impairment can impact on self-image and in turn self-esteem.

The studies which utilised specific measures to assess SM showed that when using tests that are more specific, i.e. utilising specific level concepts such as lower frequency/more abstract items or measuring reaction times on SM tasks, all participants were impaired compared with their performance on non-semantic tasks (Lambon Ralph et al., 2012). Even on simple concept tests, the patients had reaction times that were twice that of controls (Wilkins & Moscovitch, 1978; Lambon Ralph et al., 2012). However, a limitation of these studies is that no pre-surgery data was available as a comparison.

Only two studies in this review provide evidence for SM impairments post-surgery. This finding could be due to differences in testing materials and a paucity in the evidence base. It may also be due to lack of sensitivity across measures to semantic impairment. EM and naming are routinely assessed in TLE using structured neuropsychological batteries (Jones-Gotman, Harnadek, & Kuba, 2000). Generally comprehension and semantic memory is not assessed in TLE (Giovagnoli et al., 2005). In the literature there is an opinion that naming impairments may reflect SM impairments (Mayeux, Brandt, Rosen & Benson,1980; Giovagnoli et al., 2005; Drane et al., 2008); however only one study has probed this directly (Lambon Ralph et al., 2012).

Of the 12 studies reviewed, two studies were only tangentially relevant to this review as the researchers did not actually report memory impairment but change in activations as imaging technology (fMRI; functional Magnetic Resonance Imaging) was employed to assess functional activations (Koylu et al., 20008; Kim et al., 2010). However, they were included based on the inclusion criteria and provided theoretical insights into the semantic system. The authors concluded that fMRI of SM tasks may be useful in predicting postoperative verbal

memory in TLE, as activations are associated with several memory modalities. These studies provide evidence for the role of the temporal lobe in SM and for functional reorganisation.

The complexity of epilepsy presents a challenge for researchers; therefore many factors need to be considered when drawing any inferences. Overall, the above studies have contributed to an area that is vital; the quality is generally robust though the outcome is varied. Drawing firm conclusions based on these results and the application of these results to the population of retractable TLE are discussed.

5.1 Key findings

This review has highlighted key papers that address the effects of surgical intervention on SM in adults with TLE. From the 12 studies identified, two studies found no evidence of semantic memory impairment and two provided evidence for reorganisation of SM networks; one study was inconclusive, and five studies looked at attributes of SM, for example, category naming and fluency. Two studies found an association between surgery for TLE and SM impairment post surgically. The results of this review are difficult to conclude as a whole, as only two studies provided firm evidence for SM impairment post-surgical resection for TLE. These two studies were good quality studies which received over 70% on the quality score, and addressed SM directly. Overall, the findings of this review support the literature regarding the role of the anterior temporal lobes in SM. The review found that few studies assessed SM impairment directly, with the majority of studies focusing on the broader context of the declarative memory system and specific semantic processing concepts. It also found that SM was assessed using different components of conceptual knowledge, such as naming and fluency; only one study looked across a range to gain a global picture (Lambon Ralph et al., 2012). The aim of this review was not to focus on individual concepts such as naming difficulties, as such impairments are already established in the literature (Ives-Deliperi & Butler, 2012). This review highlights that certain tests used in research studies (Jefferies & Lambon Ralph, 2006; Lambon Ralph et al., 2012) may be more appropriate as tests of SM, and can assist identification of impairments

which are missed by standard clinical measures. However these tests need to be further standardised to make the transition from research to practice. A number of methodological limitations were highlighted. There was no consistency in the use of subjective and objective measures for assessing SM. Studies did not routinely use subjective measures, and only one study validated their findings with self-report measures (Ellis et al., 1989). As a whole, the results of this review suggest that surgery in TLE may be as important a risk factor for SM as it is considered to be for EM.

5.2 Suggestions for future research

Appraisal of the current literature into the effects of surgical resection on SM highlighted some key papers with strengths and limitations. Firstly as there is a lack of cohesiveness in the evidence presented, more studies are needed to determine the impact of surgery on SM in TLE. This would add to the small body of research that has appeared as a result of the growing evidence base from other neurological conditions and neuroscience studies. It provides the opportunity to study a homogenous sample, with an identifiable anatomical structure subject to en-block resection. It would be crucial to account for sclerosis pre and post-surgery as the greatest risk to memory is posed to those with non-sclerotic tissue removal (Hermann et al., 1994; Davies et al., 1998).

One of the important limitations of most of the studies in this review is the lack of a treatment as usual arm in order to compare the effects of SM. In this review, half of the studies employed a pre-and-post-surgical design. It is recommended that these studies include longer follow-up periods, ruling out disparities due to fundamental specifics versus reorganisation of the language system in intractable epilepsy (Devinsky et al., 1993). Future research could also determine the differential effects on memory based on the tests employed and other factors that are intrinsic to surgery of anatomical structures, for example, the type of surgery, the volume resected, and the structures resected, all factors that were perhaps more difficult to ascertain prior to modern brain imaging. Secondly, studies need to consider the long-term impact of epilepsy on the brain which may have already reduced the contribution of these structures. Other considerations

may be related to the recruitment process. Most of the reviewed studies recruited their samples from specialist clinics, which may not be representative of the total pharmacoresistant TLE population suitable for surgery.

Some of the lack of cohesive evidence can be attributed to the field of neuropsychology and the disparity in testing. Although memory tests have been developed over the years for specific groups, the measures most consistently employed are standardised measures such as the Boston Naming Test (BNT) and the Californian Verbal Learning Test (CVLT). This is mainly because these tests are widely available and a wide range of norms is available. However, there are tests which utilise a broader range of stimuli and need to make the transition from research tool to clinical use.

Some of the studies in this review focused on SM using measures that ranged across both clinical and research practice (Lambon Ralph et al., 2012); the test/stimuli choice of other studies was less broad and perhaps less sensitive. Future studies should justify their choice of test material clearly when selecting test batteries for clinical studies. Tests developed in SM research in other neurological conditions could increase diagnostic accuracy (Bozeat et al., 2000; Adlam et al., 2006; Jefferies & Lambon Ralph, 2006) and monitor progression.

In the literature, anomia has been described as a mild form of SM impairment (Lambon Ralph, McClelland, Patterson, Galton & Hodges, 2001). In non-aphasic TLE patients, anomia has been suggested as a marker for SM impairment (Davies et al., 1998; Antonucci, Beeson, Labiner & Rapcsak, 2008). In clinical practice, utilising measures of naming is recommended as a useful tool in measuring SM (Sawrie et al., 2000) this can lead to further exploration.

In this review there was limited use of self-report measures; a recommendation would be for more studies to employ self-report as well as objective measures, to enable corroboration of results.

5.3 Clinical implications

Overall the findings of this review are mixed, with two studies suggesting that SM is impaired post resection in TLE, and others indicating semantic processing deficits post-surgery. Conceptual knowledge (SM) is an important factor in an individuals' identity and sense of self (Patterson, Nestor & Rogers, 2007), therefore patients should be fully informed of the risks of post-surgical SM impairment as part of the current protocol to aid informed choice. This recommendation is made with caution as the measures used in the two studies are comprehensive and perhaps more sensitive to SM. However, given the consequences of SM impairment, it seems that a careful approach should be adopted. It appears that typical neuropsychological assessment in epilepsy surgery may not be capturing aspects of conceptual knowledge supported by the ATL. Disturbances in memory can be varied and may include subtle, but important, changes for the patient's daily functioning.

An important point for clinical practice is that, standardised measures should be used in conjunction with self-reports both pre-and-post surgically. Clinically the outcome of epilepsy surgery is typically measured on the merit of seizure reduction. For some patients this may outweigh the risks. Clinical interviews are part of the pre and post-surgical process along with other standard assessments which inform language lateralisation. It is suggested that clinicians should aim to incorporate results from standard measures and self-report when offering clients feedback pre and post surgically. However, a possible difficulty with this is that some patients' need for seizure control may outweigh concerns about risks, which could lead to under reporting of symptoms.

A role for the neurosurgeon and neuropsychology may also be to provide a discussion and a brochure describing temporary and long term neuropsychological consequences, to assist informed consent. As part of the epilepsy surgery pathway in hospitals, consultation should be multidisciplinary and personalised to the individual. Evidence suggests that risk to memory is based on a host of other factors and that surgery may need to be tailored to the individual. In accordance with the Epilepsy National Institute for Health and Care Excellence (NICE) Guidelines (2004), follow up at structured periods assists in the tracking of memory problems. This would enable review and implementation of any structured interventions that may be needed from clinical psychology. Examples of

interventions may include memory rehabilitation by using external aids such as diaries and calendars or other cognitive strategies (Koorenhof, Baxendale, Smith & Thompson, 2011). Often mood issues may also contribute to memory problems (Paradiso, Hermann, Blumer, Davies & Robinson, 2001) and utilising psychological therapies such as cognitive behavioural therapy (CBT) might be beneficial (Mehndiratta & Sajatovic, 2013). Working collaboratively with speech and language therapists who have formal training in language breakdown and rehabilitation would complement the role of the clinical psychologist. However, clinical experience of the author suggests that this is often difficult due to service priorities. There remains the challenge to use appropriate testing material during standard assessment and functional imaging to guide surgery.

5.4. Limitations

A major limitation of this review is the sparse number of studies identified. The limitations of the systematic review largely reflect the shortcomings of the studies reviewed. For example, the studies utilised different approaches to assessment of SM therefore pooling of the data was not feasible.

6.0 Conclusions

There is growing evidence regarding the role of the temporal lobe in SM (conceptual knowledge) from studies across patient groups. This has provided more comprehensive ways of studying the neural basis of SM by examining word comprehension, categorisation, naming, definition, and word retrieval (Bayles & Tomoeda, 1990; Jefferies & Lambon Ralph, 2006) across modalities including spoken and written words, pictures, environmental sounds, smells and touch (Bozeat et al., 2000; Jefferies & Lambon Ralph, 2006). This knowledge is important in order to predict the effect of temporal lobe resection in TLE on memory and cognition. Temporal lobe epilepsy patients undergoing unilateral surgical resection, provide a unique opportunity into understanding the underlying role of the anterior temporal lobe in memory. The current literature on the effects of temporal lobectomy on SM in TLE is sparse and the studies available are limited; nevertheless some of the studies are of good quality. Under the label of SM studies were found which focused on one aspect of a complex system. The neuropsychological testing variation may represent the spectrum along which SM

may be assessed. In order to treat the person in a holistic manner it would be imperative to obtain corroboration with their self-reported memory difficulties. This review has added to the literature aiming to determine the role of the temporal lobes in SM in TLE. Further studies need to be conducted which employ a randomised controlled design and take into account important variables from the current literature. This includes designing studies with neuropsychological tests that are both standardised and self-report in nature, with a clear rationale for choice of measures.

References

Adlam, A.L.R., Patterson, K., Rogers, T.T., Nestor, P.J., Salmond, C.H., Acosta-Cabronero, J., & J.R., Hodges. (2006). Semantic dementia and fluent primary progressive aphasia: two sides of the same coin? *Brain*, 129, 3066–80.

All-Party Parliamentary Group on Epilepsy (2007). *The Human and Economic Cost of Epilepsy in England: Wasted Money, Wasted Lives.* London: APPG on Epilepsy.

Antonucci, S.M., Beeson, P.M., Labiner, D.M., Rapcsak, S.Z. (2008). Lexical retrieval and semantic knowledge in patients with left inferior temporal lobe lesions. *Aphasiology.* 22, 281–304.

Bayles, K.A., & Tomoeda, C.K. (1990). Naming and categorical knowledge in Alzheimer's disease: The process of semantic memory deterioration. *Brain & Language.* 39, 498-510.

Baxendale, S., & Thompson, P., (2010). Beyond localisation: The role of traditional neuropsychological tests in an age of imaging. *Epilepsia.* 51, 2225-2230.

Bell, B.D., Davies, K.G., Hermann, B.P., Walters, G., (2000). Confrontation naming after anterior temporal lobectomy is related to age of acquisition of the object names. *Neuropsychologia*, 38, 83-92.

Berthier, M.L. (2001). Unexpected brain-language relationships in aphasia: evidence from transcortical sensory aphasia associated with frontal lobe lesions. *Aphasiology,* 15, 99–130.

Benton, A. L., & Hamsher, K. (1989). *Multilingual aphasia examination*. Iowa City, IA: AJA Associates.

Binder, J.R., Frost, J.A., Hammeke, T.A., Cox, R.W., Rao, S.M., & Prieto,T., (1997). Human brain language areas identified by functional magnetic resonance imaging. *J. Neurosci.* 17, 353–362.

Bozeat, S., Lambon Ralph, M.A., Patterson, K., Garrard, P., & Hodges, J.R. (2000). Non-verbal semantic impairment in semantic dementia. *Neuropsychologia*. 38, 1207–1215.

Browne, T.R., & Holmes, G.L. (2008). Epilepsy definitions and background. (Eds) *Handbook of Epilepsy* (pp.1-20). Philadelphia, PA: Lippincott Williams & Wilkins.

Boxer, A.L., Rankin, K.P., & Miller, B.L. (2003). Cinguloparietal atrophy distinguishes Alzheimer.s disease from semantic dementia*. Archives of Neurology*. 60,949-956.

Collins, A. M., & Quillian, M. R. (1969). Retrieval time from semantic memory. *Journal of Learning and Verbal Behavior*, 8, 240-247.

Commission on Classification and Terminology of the International League Against Epilepsy.(1989). Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia.* 30, 389-99.

Carol, J.B., & White, M.N., (1973). Word frequency and age of acquisition as determiners of picture naming latency. *Q.Jl.exp.Psychol*. 25, 85-95.

Duffau H, Capelle L, Denvil D, Sichez N, Gatignol P, Lopes M, et al.(2003).Functional recovery after surgical resection of low grade gliomas in eloquent brain: hypothesis of brain compensation. *J Neurol Neurosurg Psychiatr* .74, 901–7.

Damasio, H., Tranel, D., Grabowski, T., Adolphs, R., & Damasio, A. (2004). Neural systems behind word and concept retrieval. *Cognition.* 92, 179–229.

Davies, K.G., Bell, B.D., Bush, A.J., Hermann, B.P., Dohan, F.C. & Jr, Jaap, A.S. (1998). Naming decline after left anterior temporal lobectomy correlates with pathological status of resected hippocampus. *Epilepsia*. 39, 407–19.

Davies, R., Halliday, J., Xuereb c., Krill, J. & Hodges, J., (2009). The neural basis of semantic memory: Evidence from semantic dementia. *Neurobiology of Aging.* 30, 2043–2052.

Devinsky, O., Perrine, K., Llinas, R., Luciano, D.J., Dogali, M., Devinsky, O., et al. (1993). Anterior temporal language areas in patients with early onset of temporal lobe epilepsy. *Annals of Neurology*. 34, 727–732.

Drane, D.L., Ojemann, G.A., Aylward, E., Ojemann, J.G., Johnson, C.L., Silbergeld, D.L., Miller, J.W., & Tranel, D. (2008). Category-specific naming and recognition deficits in temporal lobe epilepsy surgical patients. *Neuropsychologia*. 46, 1242-1255.

Eichenbaum, H. (2000). A cortical hippocampal system for declarative memory. *Nature Reviews Neuroscience*.1, 41-50.

Ellis, A.W., Young, A.W., & Critchley, E.M. (1989). Loss of memory for people following temporal lobe damage.*Brain*.112,1469-83.

Engel, J., Cascino, G.D., & Shields, W.D. (1998). Surgically remediable syndromes. In: Engel, J.,Pedley, T.A., (Eds). *Epilepsy - a comprehensive textbook.* (pp.1687). Philadelphia: Lippincott-Raven.

Engel, J., Weibe, S., French, J., Sperling, M., Williamson, P., Spencer, D., Gumnit, R., Zahn, C., Westbrook, E. & Enos, B. (2003). Practice parameter: temporal lobe and localized neocortical resections for epilepsy. *Epilepsia,* 44, 741-51.

Fisher, R.S., van Emde Boas W., Blume, W., Elger, C., Genton, P., Lee, P., & Engel, J., Jr. (2005). Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia.* 46, 470-472.

Frisk,V., & Milner, B. (1990). The role of the left hippocampus region in the acquisition and retention of story content. *Neuropsychologia.* 28, 349–359.

Fodor, J. A. (1983). *The Modularity of Mind.* Cambridge, Mass: The MIT Press.

Galton, F. (1883). *Enquiries into human faculty and its development.* London: Macmillan.

Giffard, B., Desgranges, B., Nore-Mary, F., Lalevee, C., de la Sayette, V., Pasquier, & F., Eustache, F. (2001). The nature of semantic memory deficits in Alzheimer's disease: new insights from hyperpriming effects. *Brain*. 124, 1522–1532.

Giovagnoli AR, Erbetta A, Villani F, Avanzini G. (2005). Semantic memory in partial epilepsy: verbal and non-verbal deficits and neuroanatomical relationships. *Neuropsychologia.* 43, 1482–92.

Greenhalgh, T. (2001), *How to read a paper: the basics of evidence based medicine / Trisha Greenhalgh.* BMJ Books.

Grossman, M. (2002). Frontotemporal dementia: A review. *Journal of the International Neuropsychological Society*. 8, 566-583.

Hanning, C.D.(2005). Postoperative cognitive dysfunction. *British Journal of anaesthesia*. 95, 82-87.

Hermann, B.P., Wyler A.R., Somes G., (1991). Language Function following anterior temporal lobectomy*. J Neurosurg,* 74, 560-66.

Hermann, B. P., Wyler, A. R., Somes, G., Dohan, F. C., & Clement, L. (1994). Declarative memory following anterior temporal lobectomy in humans. *Behavioral Neuroscience.* 108,3-10.

Hermann, B.P., Seidenberg, M., Haltiner, A., Wyler, A.R. (1995). Relationship of age at onset, chronologic age, and adequacy of preoperative performance to verbal memory change after anterior temporal lobectomy. Epilepsia. 36, 137–145.

Hermann B.P., Seidenberg M., Schoenfeld J., Davies K. (1997). Neuropsychological characteristics of the syndrome of mesial temporal lobe epilepsy. *Arch Neurol.* 54, 369–76.

Hermann, B.P., Perrine, K., Cheluene, G.J., Barr, W., Loring, D.W., Strauss, E.,Trenerry, M.R., & Westerveld, M. (1999). Visual confrontation naming following

left anterior temporal lobectomy: A comparison of surgical techniques. *Neuropsychology*, 13, 3-9.

Hermann, B.P., & Jacoby, A. (2009). The psychosocial impact of epilepsy in adults. *Epilepsy Behav.* 15, S11-S16.

Higgins J, P,T., Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hodges, J.R., Patterson,K,. Oxbury, S., & Funnell, E. (1992). Semantic dementia. Progressive fluent aphasia with temporal lobe atrophy. *Brain,* 115,1783-1806.

Hodges, J.R., Graham, N., & Patterson, K. (1995) Charting the progression in semantic dementia: implications for the organisation of semantic memory. *Memory.*3, 463–495.

Ives-Deliperi, V.L. & Butler, J.T. (2012). Naming outcomes of anterior temporal lobectomy in epilepsy patients: A systematic review of the literature. *Epilepsy & Behaviour.* 24, 194-198.

Jefferies, E., & Lambon Ralph, M.A. (2006). Semantic impairment in stroke aphasia versus semantic dementia: a case-series comparison. *Brain*. 129,2132–47.

Jones-Gotman, M., Harnadek, M.C., & Kubu, C.S., (2000). Neuropsychological assessment for temporal lobe epilepsy surgery*. Can J Neurol Sci.* 1, S39-S43.

Kanwisher, N. (2010). Functional specificity in the human brain: A window into the functional architecture of the mind. *PNAS.* 107, 1-8.

Kaplan, E., Goodglass, H., & Weintraub, S. (1983). *Boston Naming Test.* Philadelphia: Lea & Febiger.

Kapur, N., Barker.S., Burrows,E.H., Ellison,J.B., IllisK.S., Colburn,C., Wilson.B., et al (1994). Herpes Simplex encephalitis: Long term magnetic resonance imaging and neuropsychological profile. *J Neurol Neurosurg pasychiatry*, 57, 1334-1342.

Keidel JL, Welbourne SR, Lambon Ralph MA.(2010). Solving the paradox of the equipotential and modular brain: a neurocomputational model of stroke vs. slow-growing glioma. *Neuropsychologia.* 48, 1716–24.

Kho, K.H., Indefrey, P., Hagoort, P., van Veelen, C.W.M., van Rijen, P.C., & Ramsey, N.F. (2008). Unimpaired sentence comprehension after anterior temporal cortex resection. *Neuropsychologia*. 46, 1170–8.

Kim, J.H., Lee, M.J., Kang, E., Kim, J.S., Song, I.C., & Chung, C.K. (2010) Functional Reorganization Associated with Semantic Language Processing in Temporal Lobe Epilepsy Patients after Anterior Temporal Lobectomy : A Longitudinal Functional Magnetic Resonance Image Study. *J Korean Neurosurg Soc*. 47, 17-25.

Kitchenham, B. (2004). *Procedures for Performing Systematic Reviews*. Department of Computer Science, Keele University .

Koorenhof, L., Baxendale, S., Smith., N & Thompson., P. (2012). Memory rehabilitation and brain training for surgical temporal lobe epilepsy patients: A preliminary report. Seizure. 21, 178-182.

Köylü, B., Walser, G., Ischebeck, A., Ortler, M., & Benke, T.(2008). Functional imaging of semantic memory predicts postoperative episodic memory functions in chronic temporal lobe epilepsy. *Brain Research*. 1223, 73-81.

Kwan, P., & Brodie, M.J. (2000) “Early identification of refractory epilepsy,” *The New England Journal of Medicine,* (pp. 314–319).vol. 342, no. 5.

Lambon Ralph, M.A., Sage, K.E, & Roberts, J. (2000). Classical anomia: a neuropsychological perspective on speech production. *Neuropsychologia*. 38, 2.

Lambon Ralph, M.A., McClelland, J.L., Patterson, K., Galton, C.J., Hodges, J.R. (2001). No right to speak? The relationship between object naming and semantic impairment: neuropsychological abstract evidence and a computational model. *J Cogn Neurosci.* 13, 341–56.

Lambon Ralph, M.A., & Patterson, K. (2008). Generalization and Differentiation in Semantic Memory: Insights from Semantic Dementia. *Ann. N.Y. Acad. Sci*, 1124, 61-76.

Lambon Ralph,M.A., Ehsan, S., Baker, G.A. & Rogers, T.T. (2012). Semantic memory is impaired in patients with unilateral anterior temporal lobe resection for temporal lobe epilepsy. *Brain*, 135, 242-258.

Martin, R.C., Loring, D.W., Meador, K.J., & Le, G.P. (1990). The effects of lateralised temporal lobe dysfunction on normal and semantic word fluency. *Neuropsychologia*.28, 823-829.

Martin, R.C., Sawrie, S.M., Roth, D.L., Gilliam, F.G., Faught, E., Morawetz, R.B., & Kuzniecky, R. (1998). Individual memory change after anterior temporal lobectomy: a base rate analysis using regression-based outcome methodology. *Epilepsia.* 39, 1075–82.

Mayeux, R., Brandt, J., Rosen, J., & Benson, D.F. (1980). Interictal memory and language impairment in temporal lobe epilepsy. *Neurology.* 30, 120-125.

Mehndiratta, P., & Sajatovic, M. (2013). Treatments for patients with comorbid epilepsy and depression: a systematic literature review. *Epilepsy Behaviour*. 28, 36-40.

Messas C.S., Mansur L.L., & Martins Castro L.H. (2008) Semantic memory impairment in temporal lobe epilepsy associated with hippocampal sclerosis. *Epilepsy & Behaviour*; 12,311-316.

Mummery, C.J., Patterson, K., Wise, R.J.S., Price, C..J., & Hodges, J.R. (1999). Disrupted temporal lobe connections in semantic dementia. *Brain*.122, 61–73

Mummery, C. J., Patterson, K., Price, C.J., Ashburner, J., Frackowiak,R.S.J, & Hodges, J. (2000). A voxel-based morphometry study of semantic dementia: relationship between temporal lobe atrophy and semantic memory. *Ann. Neurol.* 47, 36–45.

Neary, D., Snowden, J.S., Bowen, D.M., Sims, N.M., Mann, D. M., Benton, J. S., Northen. B., Yates, P. O. & Davison, A. N. (1986). Neuropsychological syndromes

in presenile dementia due to cerebral atrophy. *J Neurol Neurosurg Psychiatry.* 49,163–174.

Nestor P.J., Fryer. T.D., & Hodges, J.R. (2006). Declarative memory impairments in Alzheimer's disease and semantic dementia. *Neuroimage.* 30:1010-1020.

NICE The epilepsies: diagnosis and management of the epilepsies in adults and children in primary and secondary care. *National Institute for Clinical Excellence (NICE) Clinical Guideline*. January, 2012.

Ojemann, G, A., & Valiante, T. (2006). Resective surgey for temporal lobe epilepsy. In J.W.Miller & D.L.SIlbergeld (Eds.), *Epilepsy surgery: Principles and controversy* (pp. 403-413). New York: Taylor and Francis.

Paradiso, S., Hermann, B.P., Blumer, D., Davies, K., & Robinson, R.G. (2001). Impact of depressed mood on neuropsychological status in temporal lobe epilepsy. *J Neurol Neurosurg Psychiatry.* 70, 180-185.

Patterson, K., Nestor, P., & Rogers, T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature Reviews Neuroscience,* 8, 976-987.

Petticrew M, & Roberts, H. (2006). *Systematic reviews in the social sciences. A practical guide*. Blackwell Publishing Ltd.

Piazzini, A., Cannevini, M.P., Maggiori, G., & Canger, R. (2001). Depression and anxiety on patients with epilepsy. *Epilepsy Behav*. 5, 481-489.

Pobric, G.G., Jefferies, E., & Lambon Ralph, M.A. (2007). Anterior temporal lobes mediate semantic representation: Mimicking semantic dementia by using rTMS in normal participants. *PNAS*, 104, 20137-20141.

Public Health Resource Unit (2006). *CASP Appraisal Tools*. Retrieved from http://www.sph.nhs.uk/sph-files/casp-appraisal-tools

Quillian, M. R. (1968). Semantic memory. In M. Minsky (Ed.), *Semantic information processing.* Cambridge, MA: MIT Press.

Rogers, T.T., Lambon Ralph, M.A., Garrard, P., Bozeat, S., McClelland, J.L., Hodges, J.R., Patterson., K., et al. (2004).The structure and deterioration of semantic memory: a neuropsychological and computational investigation. *Psychol Rev.* 111, 205–35.

Rogers, T. T., Hocking, J., Noppeney, U., Mechelli, A., Gorno-Tempini,M.L, Patterson, K., & Price, C.J*. (2006).* Anterior temporal cortex and semantic memory: reconciling findings from neuropsychology and functional imaging. *Cogn. Affect.Behav. Neurosci.* 6, 201–213.

Sawrie, S.M., Martin, R.C., Gilliam, F.G., Faught, E., Maton, B., Hugg, J.W., Bush, N., Sinclair, K. & Kuzniecky, R.I. (2000). Visual confrontation naming and hippocampal function. A neural network study using quantitative 1H magnetic resonance spectroscopy. *Brain.* 123, 770-780

Schmolck, H., York, M., Verma, A., Goldsmith, I., Yosher, D., Levin, H., Foreman, P., Mizrahi, E., & Schulz. ((2005) Impaired semantic memory in temporal lobe epilepsy –what is the role of anterior temporal lobectomy? Poster presented at Annual meeting of the American Epilepsy Society.

Schuele, S.U., & Luders, H.O. (2008). Intractable epilepsy: management and therapeutic alternatives. *Lancet Neurology*, 6, 514-24.

Schwarz, M., & Pauli, E. (2009). Postoperative speech processing in temporal lobe epilepsy: functional relationship between object naming, semantics and phonology. *Epilepsy & Behavior.* 16, 629–633.

Scott, K.R. & Barrett, A.M. (2007). Dementia syndromes: evaluation and treatment. *Expert Rev Neurother*. 7, 407-422.

Shallice, T. (1988). *From neuropsychology to mental structure.* Cambridge University press.

Simmons, W.K. & Martin, A. (2009). The anterior temporal lobes and the functional architecture of semantic memory. *J Int Neuropsychol Soc*. 15, 645–9.

Skucas, A.P. & Artru, A.A. (2006). Complications of Awake Craniotomies for *Epilepsy Surgery Anesthesia & Analgesia.*102, 882-887.

Snodgrass, J.G. & Vanderwart, M. (1980). A standardised set of 260 pictures: Norms for name agreement, image agreement, familiarity, and visual complexity. Journal of *Experimental psychology: Human Learning & Memory*. 6, 174-215.

Snowden, J.S., Goulding, P.J., & Neary, D. (1989). Semantic dementia: a form of circumscribed cerebral atrophy. *Behavioral Neurology*. 2, 167-182.

Spencer, S. & Huh, L. (2008). Outcomes of epilepsy surgery in adults and children. . *Lancet Neurology*, 7, 525-537.

Spencer, D & Burchiel, K. (2012). Selective Amgdalohippocampectomy. *Epilepsy Research and Treatment.* Review; 2012, 1-8.

Spitta Verlag. (2005) *Mehrfachwahl-Wortschatz-Intelligenztest MWT-B*. *Balingen unveränderte Aufl*.5.

Thompson P.J. (1997). Epilepsy and memory. In Cull CA, Goldstein LA (Ed.), *Clinical psychologists handbook of epilepsy: assessment and management* (pp. 35 - 53). Routledge.

Thompson, P.J. (2010). The Epilepsies. In Gurd, J., Kischka, U., and Marshall, J. (Ed.), *The handbook of clinical Neuropsychology* (pp.637-659). Oxford University press.

Tulving, E. (1972). Episodic and semantic memory. In E. Tulving &. W. Donaldson (Eds.), *Organization of memory.* New York: Academic Press. pp381-403.

Tulving, E. (1983). *Elements of episodic memory.* New York: Oxford University press.

Warrington, E. K. (1975). The selective impairment of SM. *Quarterly Journal of Experimental Psychology.* 27, 635-657.

Wechsler,D. (1981). *Manual for the Wechsler adult intelligence scale-revised (WAIS-R).* The Psychological Corporation, San Antonio, TX.

WAIS-IV press release". Pearson. 2008-08-28. Retrieved 2012-03-20.

Whiting P, Westwood M, Burke M, Sterne J, Glanville J. (2008) Systematic reviews of test accuracy should search a range of databases to identify primary studies. *Journal of Clinical Epidemiology.* 61: 357-64.

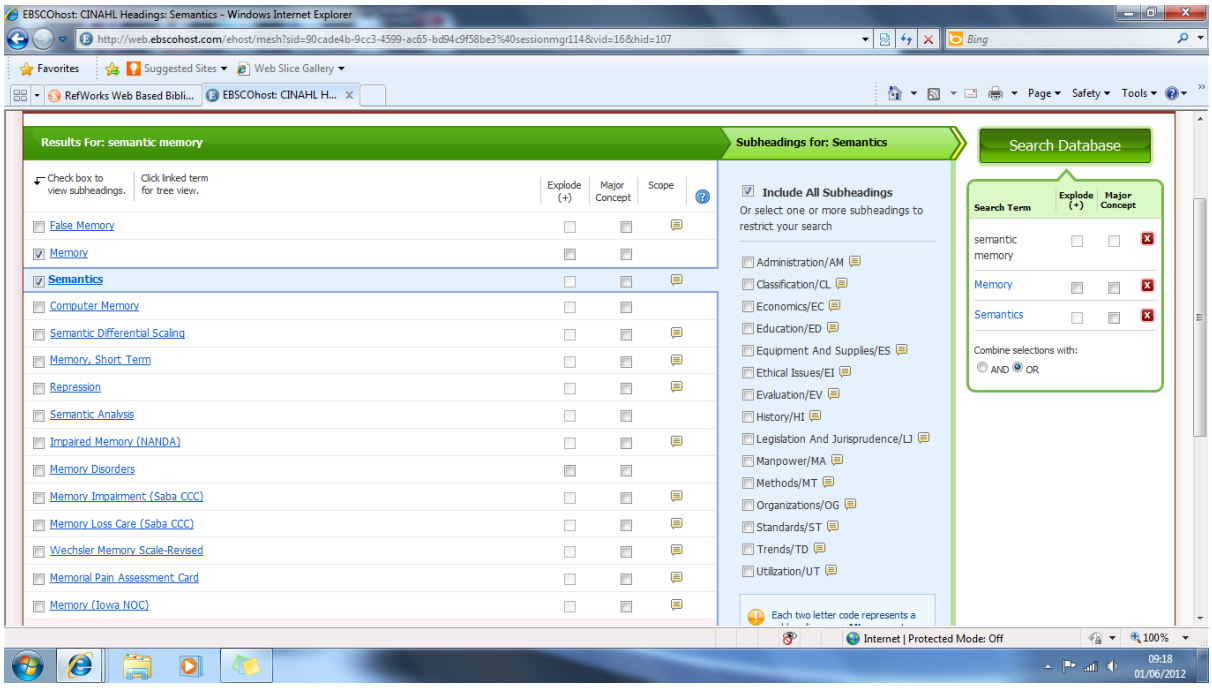
Williams, G.B., Nestor, P.J., & Hodges, J.R. (2005). Neural correlates of semantic and behavioural deficits in frontotemporal dementia. *Neuroimage,* 24, 1042-1051.

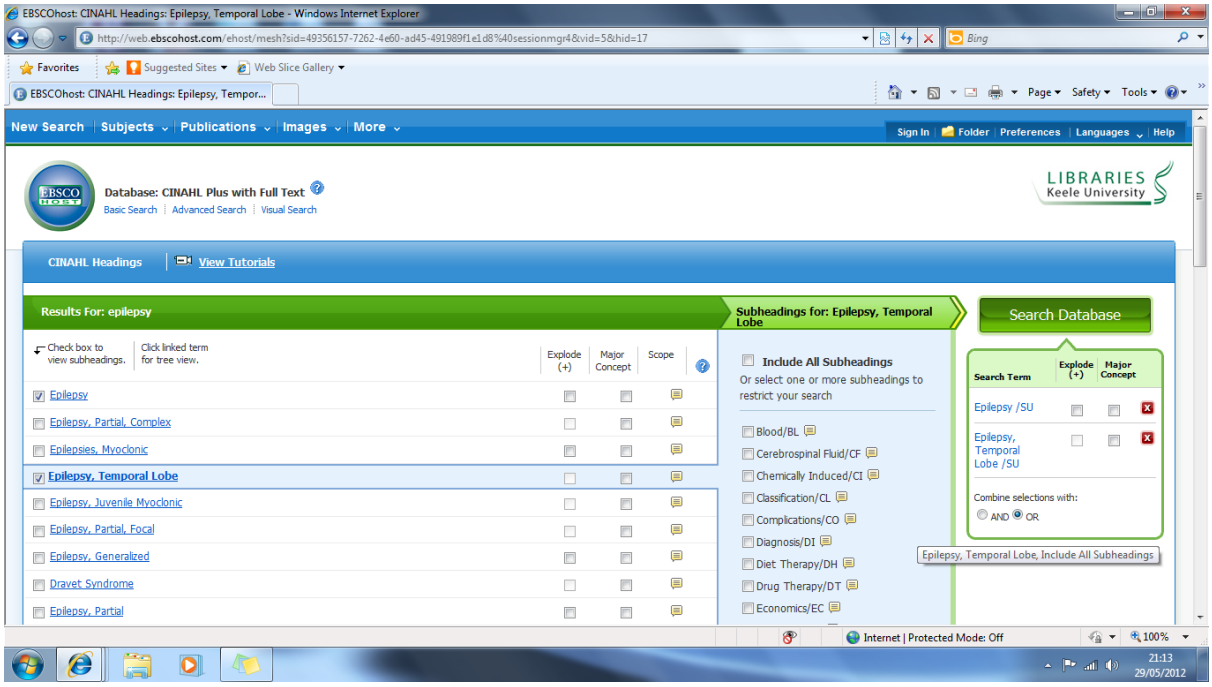
Wilkins, A. & Moscovitch, M. (1978) Selective impairment of semantic memory after temporal lobectomy. *Neuropsychologia*. 16, 73–9.

Appendix

Appendix: 1A

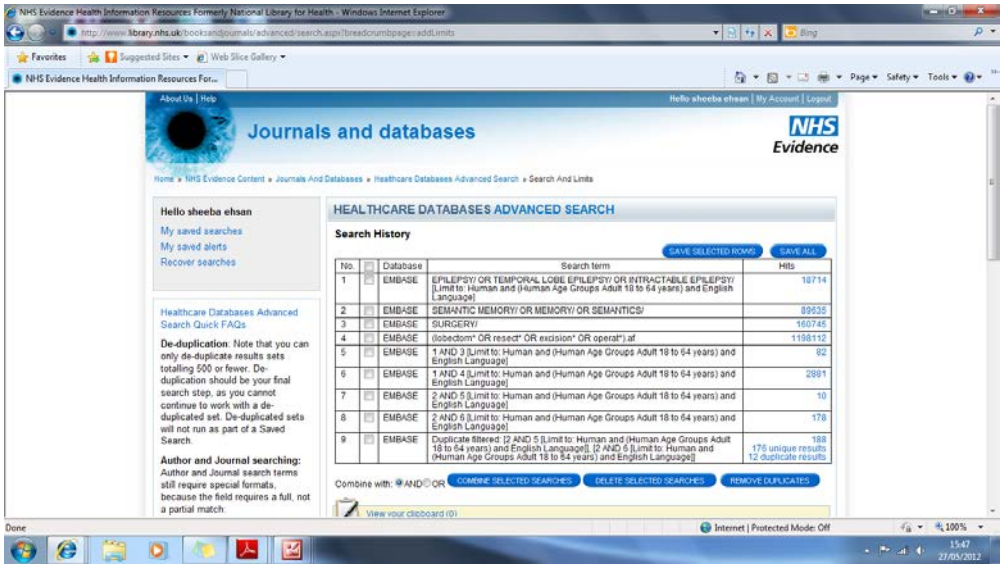
EBSCO host example of subject heading mapping for CINAHL





Appendix: 1B

EMBASE example of search combination strategy



Step 1: Search for TLE mapped to subject heading (limited to adults and English language)

Step 2: Search for SM mapped to subject heading

Step 3: Search for surgery as key word

Step 4: Search for lobectomy or resection or excision or operation in all fields

Step 5: Combination of epilepsy results and surgery

Step 6: Combination of epilepsy and other types of surgery

Step 7: Then combined with SM results

Step 8: Checked for duplicates

Appendix: 1C

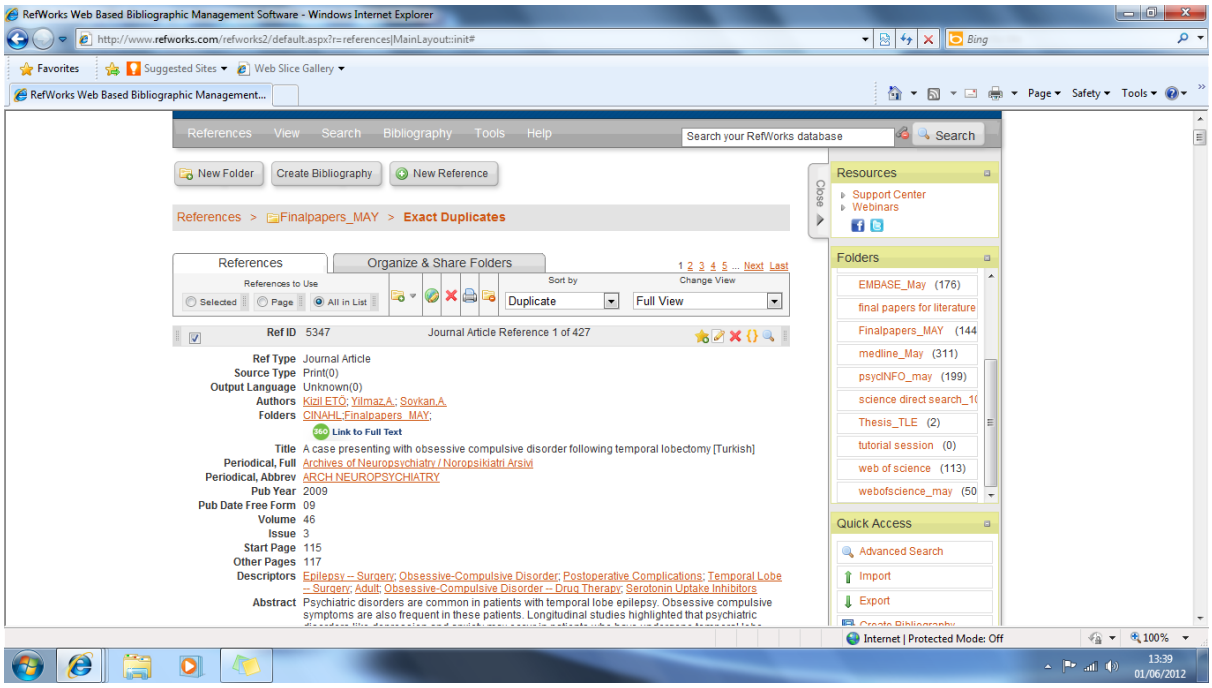
Search results for review

Database	Results (Total no of papers)
PsycInfo	199
Embase	176
MEDLINE	311
CINAHL	423
COCHRANE	27
Web of Science	506
TOTAL	**1443**

Appendix: 1D

RefWorks exact duplicates

Step 1



Step 2:

Close duplicates checked by hand = 35

Appendix: 1E

15 Item quality checklist

Question to ask of the paper
(1) Is the population clearly defined?
(2) Is the selection process of participants described?
(3) Are the objectives of the study defined?
(4) Is the design appropriate?
(5) Did it address the study question?
(6) Are the outcomes clearly defined?
(7) Did they use subjective or objective measurement?
(8) Justification of validity/reliability of measures?
(9) Are the measurement methods similar across groups?
(10) Was a control group used?
(11) Have the authors identified possible confounding factors in the sample or design?
(12) Was there a follow-up?
(13) Is the analysis described?
(14) Is the analysis appropriate?
(15) Are any limitations of the study addressed?

Criteria

Score of 1 or 0 or N/A if not applicable

Appendix: 1F

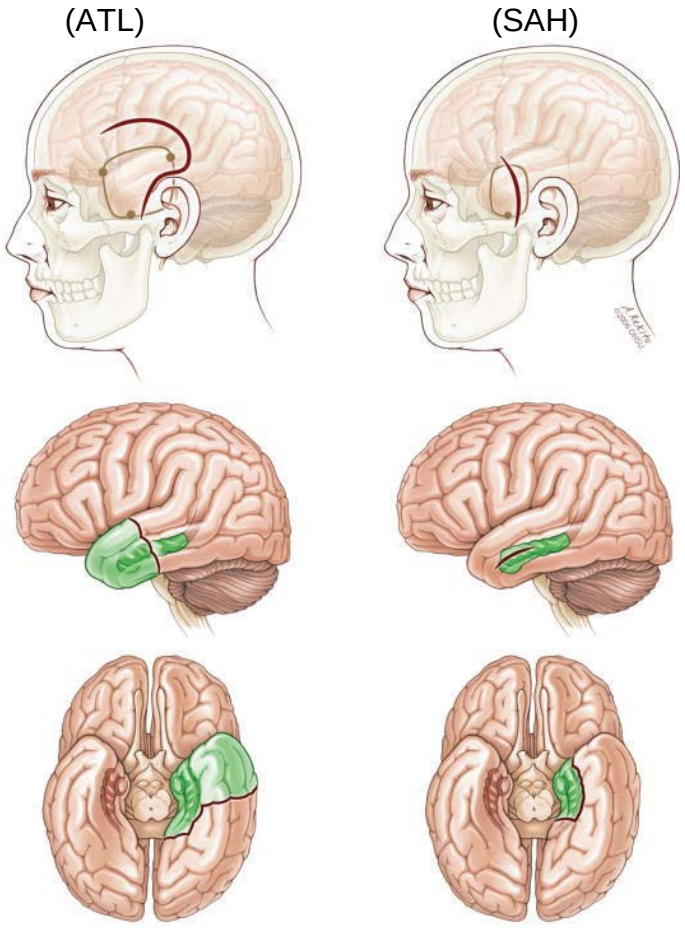
Extraction protocol

Title	
Author	
Year of publication	
Study objectives	
Design	
Measures of memory	
Sample size	
Key findings	

Appendix: 1G

Surgery type

Comparison of anterior temporal lobectomy and selective amygdalohippocampectomy surgery; (Figure taken from Spencer & Burchiel, 2011).



Surgery type	Resection
Standard anterior temporal lobectomy (ATL)	Hippocampus and parahippocampal gyrus (Mesial structures), limited excision of lateral neocortex
Selective amygdalo-hippocampectomy (SAH)	Mesial structures without neocortical resection

Appendix: 1H

Summary for figure 1

(1) 1443 papers were screened using the bibliographic software Refworks for duplicates (Appendix 4) and 462 duplicates were removed. (2) The 981 remaining studies contained a broad range of papers looking at memory, epilepsy and surgery (see Figure 1 for details of selection process). The titles of these 981 studies were then searched in order to exclude any studies that clearly did not fit the inclusion/exclusion criteria broadly, excluding 536 studies. (3) The initial elimination process left 445 studies which were screened by reading the titles and abstracts. Papers which focused on epilepsy in general or as a result of other factors e.g. tumours, and the impact of type of surgery or medication on memory (172 studies) were eliminated. (4) For the remaining 273 studies, articles in full were obtained, screened and separated according to the type of memory reported. At this stage only studies that focused on semantics, SM or verbal memory in TLE were retained, eliminating 247 studies. (5) The remaining 26 studies were read in full, and papers not explicitly testing for and not reporting semantic memory (17 studies) were excluded. (6) Finally, nine studies could be used for the present review (for details of the studies see Table 1). The reference sections of the selected papers were inspected and two further papers were obtained. These 11 studies plus one poster identified from the grey literature meant that a total of twelve studies were selected and are presented. The final outcome was 12 studies (11 papers and 1 poster).

Appendix 1I: Summary of TLE patient characteristics for the twelve studies

Study	Hippocampal Sclerosis report	AEDs	Years post-surgery	Resection	Seizure outcome	Lateralisation
Wilkins & Moscovitch, (1978)	No	No	1-21 years	Partial or complete removal of Heschl's gyrus (13), amygdala (20), hippocampus (18)	No	Left = 13 Right = 9
Ellis *et al.*(1989)	No	No	14 years	6.5cm anterior, sylvian fissure, hippocampus, amygdala	Yes	Right = 1
Hermann *et al.*(1994)	Yes pathology after surgery	No	6 months	4.5cm of temporal neocortex, inc the superior through to inferior temporal gyri and the fusiform gyrus, hippocampus and parahippocampus removed enbloc to the posterior margin of the cerebral peduncle	No	Left = 36 Right = 24
Hermann et al, 1995	Mesial Temporal Sclerosis (MTS)	No	6 months	Standard resection	Yes	Left = 50 Right = 51
Martin *et al* (1990)	Yes reported as structural lesions	Anticonvulsant blood levels obtained	1 week	4.3cm by 5.2cm by 4.9cm-left 4.7cm by 4.9cm by 4.9cm-right	No	Left = 15 Right = 17

Martin *et al.*(1998)	MTS IN 58%, 9% bilateral, unilateral MTS plus unilateral neocortical atrophy 15%, temporal lobe tumour 2 %, MTS plus focal temporal development malformation 5%, exclusive focal temporal dysplasia 3%, temporal lobe AVM 1%, normal MRI 8%	No	6-12 months post-surgery	Neocorticectomy of the anterior 4.5-5.5 cm of the temporal lobe, amygdala & two thirds of the hippocampus	Yes	Left = 53 Right = 48
Drane *et al.* (2008)	Yes	NO difference between groups in AEDs	1 year	Cortical resection ; table provided	Yes	TLE: Left = 10 Right = 6 Other-brain regions: Left = 3 Right = 3
Koylu *et al.* (2008)	Yes pathology after surgery	No	3-12 months	SAH (12 Left/9 Right), standard 2/3rd temporal lobe resection (1 left/3 Right), modified standard resection (1 left)	Yes	Left = 14 Right = 12
Schwarz & Pauli. (2009)	Yes	No	6 months	3cm middle & inferior temporal gyrus & removal of two-thirds of the hippocampus. Superior temporal gyrus was spared	Yes	Left = 24 Right = 34
Kim *et al.* (2010)	Yes pathology after surgery	No	1 year	En bloc ATL and SAH. Superior temporal lobe included, amygdala & 3cm of the head of the hippocampus	Yes	Left = 12 Right = 7
Schmolck et al. (2005)	No	No	2 yrs	ATL	No	Left = 9 Right = 12

Lambon Ralph *et al* (2012)	Pre surgical scan report and pathology report	No	1.5-5yrs	Yes volume resected standard en bloc	Yes	Left = 9 Right = 11

Notes: Anterior temporal lobe (ATL), selective amygdala hippocampectomy (SAH), anti-epileptic drugs (AEDs), mesial temporal sclerosis (MTS), arteriovenous malformation (AVM), magnetic resonance imaging (MRI).

Appendix 1J: Journal Guidelines

Neuropsychologia

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 1

NEUROPSYCHOLOGIA

An International Journal in Behavioural and Cognitive Neuroscience

AUTHOR INFORMATION PACK

TABLE OF CONTENTS

ISSN: 0028-3932

DESCRIPTION

Neuropsychologia is an international interdisciplinary journal devoted to experimental and theoretical contributions that advance understanding of human cognition and behavior from a neuroscience perspective. The journal will consider for publication studies that link brain function with cognitive processes, including attention and awareness, action and motor control, executive functions and cognitive control, memory, language, and emotion and social cognition. Neuropsychologia has a long history of publishing lesion-deficit studies, and these remain highly appropriate for the journal. Submission of papers describing the use of other methodologies – most notably functional and structural neuroimaging, cognitive electrophysiology, and transcranial magnetic stimulation - is strongly encouraged, however. Animal studies are also welcome, provided they have a direct and explicitly specified impact on understanding human cognition and behavior. Studies of clinical populations that are primarily descriptive or intended to elucidate a clinical disorder, or that evaluate a therapeutic intervention, are not appropriate for

the journal. Special issues and Review Papers are published regularly with the aim of providing authoritative surveys of topics of major interest.

Benefits to authors

We also provide many author benefits, such as free PDFs, a liberal copyright policy, special discounts on Elsevier publications and much more. Please click here for more information on our author services. Please see our Guide for Authors for information on article submission. If you require any further information or help, please visit our support pages: http://support.elsevier.com

AUDIENCE

Researchers in human and animal behavioural and cognitive neuroscience.

IMPACT FACTOR

2012: 3.477 © Thomson Reuters Journal Citation Reports 2013

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 2

ABSTRACTING AND INDEXING

BIOSIS

Elsevier BIOBASE

Current Contents/ASCA

Current Contents/BIOMED Database

Current Contents/Life Sciences

Current Contents/SciSearch Database

Current Contents/Science Citation Index

Current Contents/Social & Behavioral Sciences

MEDLINE®

EMBASE

Scopus

EDITORIAL BOARD

Editor-in-Chief

M.D. Rugg, Center for Vital Longevity and School of Behavioral and Brain Sciences, University of Texas at Dallas,1600 Viceroy Drive, Suite 800, Dallas, 75235, Texas, USA

Section Editors:

Action & Motor Control

T. Schenk, Neurologische Klinik, Universitätsklinikum Erlangen, Schwabachanlage 6, 91054, Erlangen, Germany

Attention & Consciousness

J. Coull, Laboratoire des Neurosciences Cognitives (UMR 7291), CNRS - Aix-Marseille University, 3 Place Victor Hugo 13331, Cedex 3, Marseille, France

Emotion & Social Neuroscience

S. Hamann, Dept. of Psychology, Emory University, 309 Psychology Building-532 Kilgo Circle, Atlanta, GA 30322,

Georgia, USA

D.H. Zald, Dept. of Psychology, PMB 407817,Vanderbilt University, 2301 Vanderbilt Palce, Nashville, TN 37240-7817, Tennessee, USA

Executive Function & Cognitive Control

M.T. Banich, Dept. of Psychology, University of Colorado, Campus Box 345, Boulder, CO 80309-0345, Colorado,USA

P. Reuter-Lorenz, Dept. of Psychology, University of Michigan, 525 East University Street, Ann Arbor, MI48109-109, Michigan, USA

Language

I. Johnsrude, Dept. of Psychology, Queen's University, 62 Arch Street, St. Catharines, K7L 3N6, Ontario, Canada

K. Watkins, Dept. of Experimental Psychology, University of Oxford, South Parks Road, Oxford, OX1 3UD, UK

Memory

K.A. Paller, Dept. of Psychology and Interdepartmental Neuroscience Program, Northwestern University,

Evanston, IL 60208-2710, Illinois, USA

M.D. Rugg, Center for Vital Longevity and School of Behavioral and Brain Sciences, University of Texas at Dallas,1600 Viceroy Drive, Suite 800, Dallas, 75235, Texas, USA

Perception

M. Murray, Dept. of Clinical Neurosciences, Div. of Neurology,Centre Hospitalier Universitaire Vaudois Lausanne(CHUV), Rue du Bugnon 46, Radiology-CIBM BH08.078, 1011, Lausanne, Switzerland

Editorial Advisory Board

R. Adolphs, Pasadena, California, USA

J.P. Aggleton, Cardiff, UK

D. Ansari, London, Ontario, Canada

A.R. Aron, Los Angeles, California, USA

S. Baron-Cohen, Cambridge, UK

M. Behrmann, Pittsburgh, Pennsylvania, USA

G. Berlucchi, Verona, Italy

C. Beste, Bochum, Germany

D.P. Carey, Bangor, UK

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 3

G.A. Carlesimo, Rome, Italy

M.C. Corballis, Auckland, New Zealand

M. Corbetta, St. Louis, Missouri, USA

R Cunnington, St. Lucia, Queensland, Australia

J. Decety, Chicago, Illinois, USA

A. Diamond, Waltham, Massachusetts, USA

C. Dijkerman, Utrecht, Netherlands

M. Eimer, London, UK

F. Eustache, Caen, France

G. Gainotti, Rome, Italy

G. Goldenberg, München, Germany

M.A. Goodale, London, Canada

C. Gross, Princeton, New Jersey, USA

B. Hanna-Pladdy, Atlanta, Georgia, USA

M. Harvey, Glasgow, Scotland, UK

A. Henik, Beer-Sheva, Israel

C.A. Heywood, Durham, UK

M. Jeannerod, Bron, France

N. Kanwisher, Cambridge, Massachusetts, USA

F. Karayanidis, Callaghan, New South Wales, Australia

H.O. Karnath, Tübingen, Germany

S. Kastner, Princeton, USA

G. Kerkhoff, Saarbrücken, Germany

M.D. Kopelman, London, UK

E. Ladavas, Bologna, Italy

T.M.C. Lee, Hong Kong, Hong Kong

E. Maguire, London, England, UK

A. Martin, Bethesda, Maryland, USA

C.A. Marzi, Verona, Italy

J.B. Mattingley, St Lucia, Australia

A.R. Mayes, Manchester, England, UK

M. Moscovitch, Toronto, Canada

E.A. Murray, Bethesda, Maryland, USA

T.F. Münte, Lübeck, Germany

L. Nadel, Tucson, Arizona, USA

I. Peretz, Montréal, Canada

M. Petrides, Montreal, Quebec, Canada

M.I. Posner, Eugene, Oregon, USA

V. Reid, Lancaster, England, UK

C. Semenza, Padova, Italy

M.C. Silveri, Palidoro Rome, Italy

J.S. Snowden, Salford, UK

D.T. Stuss, Toronto, Ontario, Canada

C.M. Temple, Colchester, UK

D. Tranel, Iowa City, Iowa, USA

G. Vallar, Milano, Italy

M. Verfaellie, Boston, Massachusetts, USA

A. Wagner, Stanford, California, USA

C.W. Wallesch, Elzach, Germany

L. Weiskrantz, Oxford, UK

S. Zihl, München, Germany

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 4

GUIDE FOR AUTHORS

Your Paper Your Way

ypyw-gfa-banner.gifyour paper your way

BEFORE YOU BEGIN

Ethics in publishing

For information on Ethics in publishing and Ethical guidelines for journal publication see

http://www.elsevier.com/publishingethics and http://www.elsevier.com/journal-authors/ethics.

Conflict of interest

All authors are requested to disclose any actual or potential conflict of interest including any financial,

personal or other relationships with other people or organizations within three years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work. See also http://www.elsevier.com/conflictsofinterest. Further information and an example of a Conflict of Interest form can be found at:
http://help.elsevier.com/app/answers/detail/a_id/286/p/7923.

Submission declaration

Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, see http://www.elsevier.com/postingpolicy), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere including electronically in the same form, in English or in any other language, without the written consent of the copyright-holder.

Changes to authorship

This policy concerns the addition, deletion, or rearrangement of author names in the authorship ofaccepted manuscripts: Before the accepted manuscript is published in an online issue: Requests to add or remove an author,or to rearrange the author names, must be sent to the Journal Manager from the corresponding author of the accepted manuscript and must include: (a) the reason the name should be added or removed, or the author names rearranged and (b) written confirmation (e-mail, fax, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors,this includes confirmation from the author being added or removed. Requests that are not sent by the corresponding author will be forwarded by the Journal Manager to the corresponding author, who must follow the procedure as described above. Note that: (1) Journal Managers will inform the Journal

Editors of any such requests and (2) publication of the accepted manuscript in an online issue issuspended until authorship has been agreed.After the accepted manuscript is published in an online issue: Any requests to add, delete, or rearrange author names in an article published in an online issue will follow the same policies as noted above and result in a corrigendum.

Copyright

This journal offers authors a choice in publishing their research: Open Access and Subscription.

For Subscription articles

Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' (for more information on this and copyright, see http://www.elsevier.com/copyright). An e-mail will be sent to the corresponding author confirming receipt of the manuscript together with a 'Journal Publishing Agreement' form or a link to the online version of this agreement.Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution and for all other derivative works, including compilations and translations (please consult http://www.elsevier.com/permissions). If excerpts from other copyrighted works are included, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has preprinted forms for use by authors in these cases: please consult

http://www.elsevier.com/permissions.

For Open Access articles

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 5 Upon acceptance of an article, authors will be asked to complete an 'Exclusive License Agreement' (for more information see http://www.elsevier.com/OAauthoragreement). Permitted reuse of open access articles is determined by the author's choice of user license (see

http://www.elsevier.com/openaccesslicenses).

Retained author rights

As an author you (or your employer or institution) retain certain rights. For more information on

author rights for:

Subscription articles please see

http://www.elsevier.com/journal-authors/author-rights-and-responsibilities.

Open access articles please see http://www.elsevier.com/OAauthoragreement.

Role of the funding source

You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should be stated.

Funding body agreements and policies

Elsevier has established agreements and developed policies to allow authors whose articles appear in journals published by Elsevier, to comply with potential manuscript archiving requirements as specified as conditions of their grant awards. To learn more about existing agreements and policies please visit

http://www.elsevier.com/fundingbodies.

Open access

This journal offers authors a choice in publishing their research:

Open Access

• Articles are freely available to both subscribers and the wider public with permitted reuse

• An Open Access publication fee is payable by authors or their research funder

Subscription

• Articles are made available to subscribers as well as developing countries and patient groups through our access programs (http://www.elsevier.com/access)

• No Open Access publication fee

All articles published Open Access will be immediately and permanently free for everyone to read and download. Permitted reuse is defined by your choice of one of the following Creative Commons user licenses: Creative Commons Attribution (CC BY): lets others distribute and copy the article, to create extracts, abstracts, and other revised versions, adaptations or derivative works of or from an article (such as a translation), to include in a collective work (such as an anthology), to text or data mine the article, even for commercial purposes, as long as they credit the author(s), do not represent the author as endorsing their adaptation of the article, and do not

modify the article in such a way as to damage the author's honor or reputation. Creative Commons Attribution-NonCommercial-Share Alike (CC BY-NC-SA): for non-commercial purposes, lets others distribute and copy the article, to create extracts, abstracts and other revised versions, adaptations or derivative works of or from an article (such as a translation),to include in a collective work (such as an anthology), to text and data mine the article, as long as they credit the author(s), do not represent the author as endorsing their adaptation of the article, do not modify the article in such a way as to damage the author's honor or reputation, and license their new adaptations or creations under identical terms (CC BY-NC-SA).

Creative Commons Attribution-Non Commercial-NoDerivs (CC BY-NC-ND): for non-commercial purposes, lets others distribute and copy the article, and to include in a collective work (such as an anthology), as long as they credit the author(s) and provided they do not alter or modify the article.To provide Open Access, this journal has a publication fee which needs to be met by the authors or their research funders for each article published Open Access. Your publication choice will have no effect on the peer review process or acceptance of submitted articles.

The publication fee for Open Access in this journal is $1,800, excluding taxes. Learn more about Elsevier's pricing policy: http://www.elsevier.com/openaccesspricing.

Language (usage and editing services)

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the English Language Editing service available from Elsevier's WebShop (http://webshop.elsevier.com/languageediting/) or visit our customer support site (http://support.elsevier.com) for more information.

Submission

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts source files to a single PDF file of the article, which is used in the peer-review process. Please note that even though manuscript source files are converted to PDF files at submission for the review process, these source files are needed for further processing after acceptance. All correspondence, including notification of the Editor's decision and requests for revision, takes place by e-mail removing the need for a paper trail.

Submission Address http://ees.elsevier.com/nsy/The Neuroscience Peer Review Consortium Neuropsychologia is a member of the Neuroscience Peer Review Consortium (NPRC). The NPRC has been formed to reduce the time expended and, in particular, the duplication of effort by, and associated burden on reviewers involved in the peer review of original neuroscience research papers. It is an alliance of neuroscience journals that have agreed to accept manuscript reviews from other Consortium journals. By reducing the number of times that a manuscript is reviewed, the Consortium will reduce the load on reviewers and Editors, and speed the publication of research results. If a manuscript has been rejected by another journal in the Consortium, authors can submit the manuscript to Neuropsychologia and indicate that the referees' reports from the

first journal will be made available to the Editors of Neuropsychologia It is the authors' decision as to whether or not to indicate that a set of referee's reports should be forwarded from the first journal to Neuropsychologia. If an author does not wish for this to happen, the manuscript can be submitted to Neuropsychologia without reference to the previous submission. No information will be exchanged between journals except at the request of authors. However, if the original referees' reports suggested that the paper is of high quality, but not suitable for the first journal, then it will often be to an author's advantage to indicate that referees' reports should be made available. Authors should revise the original submission in accordance with the first journal's set of referee reports, Neuropsychologia and indicate that the referees' reports from the first journal be made available to the editors of Neuropsychologia. It is the authors' decision whether or not to indicate that a set of referee's reports should be forwarded from the first journal to Neuropsychologia. If an author does not wish for this to happen, the manuscript can be submitted to Neuropsychologia without reference to the previous submission. No information will be exchanged between journals except at the request of authors. However, if the original referees' reports suggested that the paper is of high quality, but not suitable for the first journal, then it will often be to an author's advantage to indicate that referees' reports should be made available. Authors should revise the original submission in accordance with the first journal's set of referee reports, Neuropsychologia and submit the paper to Neuropsychologia with a covering letter describing the changes that have been made, and informing the Editors that the authors will ask for referees' reports to be forwarded from the first Consortium journal. The authors then must contact the first journal, and ask that reviews be forwarded, indicating they have submitted to Neuropsychologia, and providing the new manuscript ID number.

The Editors of Neuropsychologia will use forwarded referees' reports at their discretion. The Editors may use the reports directly to make a decision, or they may request further reviews if they feel such are necessary. Visit http://nprc.incf.org for a list of Consortium journals, as well as further information on the scheme.

PREPARATION

The following article types are accepted:

(a) Research Reports (up to 20 printed journal pages or about 17,000 words)

(b)Reviews and Perspectives (up to 30 printed journal pages or 26,000 words). These should also provide critical accounts and comprehensive surveys of topics of major current interest within the scope of the journal.

NEW SUBMISSIONS

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts your files to a single PDF file, which is used in the peer-review process. As part of the Your Paper Your Way service, you may choose to submit your manuscript as a single file to be used in the refereeing process. This can be a PDF file or a Word document, in any format or layout that can be used by referees to evaluate your manuscript. It should contain high enough quality figures for refereeing. If you

prefer to do so, you may still provide all or some of the source files at the initial submission. Please note that individual figure files larger than 10 MB must be uploaded separately.

References

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain the essential elementsneeded to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions. If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes. Divide the article into clearly defined sections.

Figures and tables embedded in text Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file.

REVISED SUBMISSIONS

Use of word processing software Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier: http://www.elsevier.com/guidepublication). See also the section on Electronic artwork. To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

Subdivision - numbered sections Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literaturesurvey or a summary of the results.

Material and methods

Provide sufficient detail to allow the work to be reproduced. Methods already published should beindicated by a reference: only relevant modifications should be described.

Results

Results should be clear and concise.

Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published

literature.

Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations inappendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix,

Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc. Essential title page information

• Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• Author names and affiliations. Where the family name may be ambiguous (e.g., a double name), please indicate this clearly. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

• Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. Ensure that phone numbers (with country and area code) are provided in addition to the e-mail address and the complete postal address. Contact details must be kept up to date by the corresponding author.

• Present/permanent address. If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon

abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

Graphical abstract

A Graphical abstract is optional and should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership online. Authors must provide images that clearly represent the work described in the article. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. See http://www.elsevier.com/graphicalabstracts for examples. Authors can make use of Elsevier's Illustration and Enhancement service to ensure the best presentation of their images also in accordance with all technical requirements: Illustration Service.

Highlights

Highlights are mandatory for this journal. They consist of a short collection of bullet points that convey the core findings of the article and should be submitted in a separate file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point). See http://www.elsevier.com/highlights for examples.

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 9

Keywords Immediately after the abstract, provide a maximum of 6 keywords, using British spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

Database linking

Elsevier encourages authors to connect articles with external databases, giving their readers oneclick access to relevant databases that help to build a better understanding of the described research.Please refer to relevant database identifiers using the following format in your article: Database: xxxx(e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN). See http://www.elsevier.com/databaselinking for more information and a full list of supported databases.

FootnotesFootnotes should be used sparingly. Number them consecutively throughout the article. Many wordprocessors build footnotes into the text, and this feature may be used. Should this not

be the case, indicate the position of footnotes in the text and present the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

Table footnotes

Indicate each footnote in a table with a superscript lowercase letter.

Artwork

Electronic artwork

General points

• Make sure you use uniform lettering and sizing of your original artwork.

• Preferred fonts: Arial (or Helvetica), Times New Roman (or Times), Symbol, Courier.

• Number the illustrations according to their sequence in the text.

• Use a logical naming convention for your artwork files.

• Indicate per figure if it is a single, 1.5 or 2-column fitting image.

• For Word submissions only, you may still provide figures and their captions, and tables within a single file at the revision stage.

• Please note that individual figure files larger than 10 MB must be provided in separate source files.

A detailed guide on electronic artwork is available on our website:

http://www.elsevier.com/artworkinstructions.

You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

Regardless of the application used, when your electronic artwork is finalized, please 'save as' orconvert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.

TIFF (or JPG): Color or grayscale photographs (halftones): always use a minimum of 300 dpi.

TIFF (or JPG): Bitmapped line drawings: use a minimum of 1000 dpi.

TIFF (or JPG): Combinations bitmapped line/half-tone (color or grayscale): a minimum of 500 dpi is required.

Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); the resolution is too low.

• Supply files that are too low in resolution.

• Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color on the Web (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article. Please indicate your preference for color: in print or on the Web only. For further information on the preparation of electronic artwork, please see http://www.elsevier.com/artworkinstructions. Please note: Because of technical complications which can arise by converting color figures to 'gray scale' (for the printed version should you not opt for color in print) please submit in addition usable black and white versions of all the color illustrations.

Figure captions

Ensure that each illustration has a caption. A caption should comprise a brief title (not on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Number tables consecutively in accordance with their appearance in the text. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article.

References

Citation in text Please ensure that every reference cited in the text is also present in the reference list (and viceversa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication,

etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

References in a special issue

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

Reference formatting

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct. If you do wish to format the references yourself they should be arranged according to the following examples:

Reference style

Text: Citations in the text should follow the referencing style used by the American Psychological Association. You are referred to the Publication Manual of the American Psychological Association, Sixth Edition, ISBN 978-1-4338-0561-5, copies of which may be ordered from http://books.apa.org/books.cfm?id=4200067 or APA Order Dept., P.O.B. 2710, Hyattsville, MD 20784, USA or APA, 3 Henrietta Street, London, WC3E 8LU, UK. List: references should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

Examples:

Reference to a journal publication:

Van der Geer, J., Hanraads, J. A. J., & Lupton, R. A. (2010). The art of writing a scientific article.

Journal of Scientific Communications, 163, 51–59.

Reference to a book:

Strunk, W., Jr., & White, E. B. (2000). The elements of style. (4th ed.). New York: Longman, (Chapter

4).

Reference to a chapter in an edited book:

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 11

Mettam, G. R., & Adams, L. B. (2009). How to prepare an electronic version of your article. In B. S.

Jones, & R. Z. Smith (Eds.), Introduction to the electronic age (pp. 281–304). New York: E-Publishing

Inc.

Video data

Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the files in one of our recommended file formats with a preferred maximum size of 50 MB. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages at http://www.elsevier.com/artworkinstructions. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

AudioSlides

The journal encourages authors to create an AudioSlides presentation with their published article. AudioSlides are brief, webinar-style presentations that are shown next to the online article on ScienceDirect. This gives authors the opportunity to summarize their research in their own words and to help readers understand what the paper is about. More information and examples are available at http://www.elsevier.com/audioslides. Authors of this journal will automatically receive an invitation e-mail to create an AudioSlides presentation after acceptance of their paper.

Supplementary data

Elsevier accepts electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, highresolution images, background datasets, sound clips and more. Supplementary files supplied will be published online alongside the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. In order to ensure that your submitted material is directly usable, please provide the data in one of our recommended file formats. Authors should submit the material in electronic format together with the article and supply a concise and descriptive caption for each file. For more detailed instructions please visit our artwork instruction pages at http://www.elsevier.com/artworkinstructions.

3D neuroimaging

You can enrich your online articles by providing 3D neuroimaging data in NIfTI format. This will be visualized for readers using the interactive viewer embedded within your article, and will enable

them to: browse through available neuroimaging datasets; zoom, rotate and pan the 3D brain reconstruction; cut through the volume; change opacity and color mapping; switch between 3D and 2D projected views; and download the data. The viewer supports both single (.nii) and dual (.hdr and .img) NIfTI file formats. Recommended size of a single uncompressed dataset is 100 MB or less. Multiple datasets can be submitted. Each dataset will have to be zipped and uploaded to the online submission system via the '3D neuroimaging data' submission category. Please provide a short informative description for each dataset by filling in the 'Description' field when uploading a dataset. Note: all datasets will be available for downloading from the online article on ScienceDirect. If you have concerns about your data being downloadable, please provide a video instead. For more information see: http://www.elsevier.com/3DNeuroimaging.

Submission checklist

The following list will be useful during the final checking of an article prior to sending it to the journalfor review. Please consult this Guide for Authors for further details of any item. Ensure that the following items are present: One author has been designated as the corresponding author with contact details:

• E-mail address

• Full postal address

• Telephone

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 12

All necessary files have been uploaded, and contain:

• Keywords

• All figure captions

• All tables (including title, description, footnotes)

Further considerations

• Manuscript has been 'spell-checked' and 'grammar-checked'

• All references mentioned in the Reference list are cited in the text, and vice versa

• Permission has been obtained for use of copyrighted material from other sources (including the Web)

• Color figures are clearly marked as being intended for color reproduction on the Web (free of charge) and in print, or to be reproduced in color on the Web (free of charge) and in black-and-white in print

• If only color on the Web is required, black-and-white versions of the figures are also supplied for

printing purposes For any further information please visit our customer support site at http://support.elsevier.com.

AFTER ACCEPTANCE

Use of the Digital Object Identifier

The Digital Object Identifier (DOI) may be used to cite and link to electronic documents. The DOI consists of a unique alpha-numeric character string which is assigned to a document by the publisher upon the initial electronic publication. The assigned DOI never changes. Therefore, it is an ideal medium for citing a document, particularly 'Articles in press' because they have not yet received their full bibliographic information. Example of a correctly given DOI (in URL format; here an article in the journal Physics Letters B): http://dx.doi.org/10.1016/j.physletb.2010.09.059

When you use a DOI to create links to documents on the web, the DOIs are guaranteed never to change. Online proof correction

Corresponding authors will receive an e-mail with a link to our online proofing system, allowing annotation and correction of proofs online. The environment is similar to MS Word: in addition to editing text, you can also comment on figures/tables and answer questions from the Copy Editor. Web-based proofing provides a faster and less error-prone process by allowing you to directly type your corrections, eliminating the potential introduction of errors. If preferred, you can still choose to annotate and upload your edits on the PDF version. All instructions for proofing will be given in the e-mail we send to authors, including alternative methods to the online version and PDF. We will do everything possible to get your article published quickly and accurately - please upload all of your corrections within 48 hours. It is important to ensure that all corrections are sent back to us in one communication. Please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility. Note that Elsevier may proceed with the publication of your article if no response is received.

Offprints

The corresponding author, at no cost, will be provided with a PDF file of the article via email (the PDF file is a watermarked version of the published article and includes a cover sheet with the journal cover image and a disclaimer outlining the terms and conditions of use). For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's WebShop (http://webshop.elsevier.com/myarticleservices/offprints). Authors requiring printed copies of multiple articles may use Elsevier WebShop's

'Create Your Own Book' service to collate multiple articles within a single cover (http://webshop.elsevier.com/myarticleservices/offprints/myarticlesservices/booklets).

AUTHOR INQUIRIES

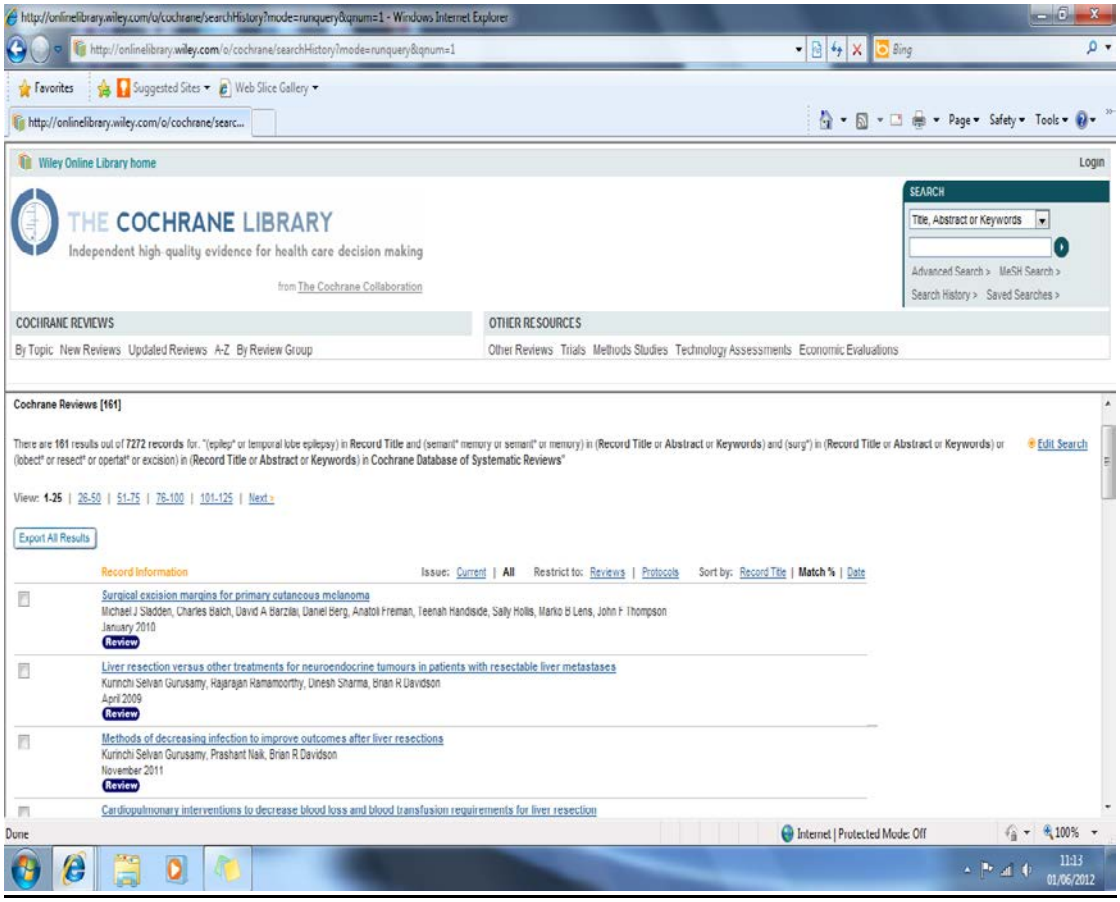
For inquiries relating to the submission of articles (including electronic submission) please visit this journal's homepage. For detailed instructions on the preparation of electronic artwork, please visit http://www.elsevier.com/artworkinstructions. Contact details for questions arising after acceptance of an article, especially those relating to proofs, will be provided by the publisher. You can track accepted articles at http://www.elsevier.com/trackarticle. You can also check our

Author FAQs at http://www.elsevier.com/authorFAQ and/or contact Customer Support via http://support.elsevier.com.

AUTHOR INFORMATION PACK 11 May 2014 www.elsevier.com/locate/neuropsychologia 13

Appendix 1J:

Cochrane library search results



Paper 2: Empirical research report

Semantic memory in temporal lobe epilepsy following unilateral resection: A tailored neuropsychological profile with self-report.

This paper has been written for submission of publication to Epilepsy & Behaviour (Appendix 2K) (The Journal of the International League Against Epilepsy)

Word count: 8541

KEY WORDS: Temporal lobe epilepsy, Surgery, Semantic Memory, Neuropsychological assessment.

Abstract

Epilepsy surgery can cause a number of cognitive deficits, which can have a detrimental impact on quality of life. These deficits can be measured by both self-report measures and formal neuropsychological testing. The objective of this study was to explore the correlation between self-reported semantic memory (SM) difficulties and a standardised SM assessment, in a sample of 20 temporal lobe epilepsy (TLE) post-surgery patients (nine left and 11 right). Self-report was also explored using quantitative content analysis in order to understand patients' experiences. In general, self-report ratings of memory were not significantly correlated with objective neuropsychological testing. Scores on a test of naming correlated with self-report. Exploration of self-report data highlighted that an equal number of left and right TLE patients reported problems in the SM. Five key themes were identified which provide an insight into participants' broader quality of life experience. Participants were more sensitive to naming impairments than other forms of SM impairments post-surgery. Self-report of naming impairments may indicate semantic processing difficulties, and therefore may be a valuable method to aid clinical assessment. Clinical neuropsychologists are well placed to offer these assessments.

1.1. Introduction

Epilepsy is a chronic neurological disorder with an incidence rate of 50 per 100,000 per annum in the United Kingdom [1]. The prevalence figure for epilepsy in the UK is 5-10 cases per 1,000 [2]. The term the ‘epilepsies’ is used in UK guidance [3] to reflect that epilepsy is a symptom of an underlying neurological disorder. The International League Against Epilepsy (ILAE) state that epilepsy refers to a group of conditions characterised by enduring seizures in the brain; an epileptic seizure is defined as a transient occurrence of signs and/or symptoms due to abnormal, excessive or synchronous neuronal activity in the brain [4]. This definition of epilepsy requires the occurrence of at least one epileptic seizure [5]. The ILAE [4, 5] classify epilepsy into seizure types and epilepsy syndromes on the basis of focal seizures (localised to a particular area of the brain) or generalised seizures which affect the whole brain.

Epilepsy can have many consequences for the individual, including a detrimental impact on education, employment, relationships, psychosocial and psychological difficulties including, anxiety, depression, social discrimination and misconceptions or stigma about the disorder [2]. For example, individuals may experience anxiety about activities due to the possibility of a seizure, and avoid disclosing their difficulties to others due to perceived or actual societal stigma. Clinical psychology can provide a vital role in the management of epilepsy, as recognised by the UK NICE guidance [3]. Psychological interventions such as relaxation techniques and cognitive behaviour therapy have been associated with an improved quality of life [3]. Neuropsychological impairments in epilepsy are common due to an interplay of various factors, including seizure frequency and severity, psychological difficulties, medication and underlying pathology. This paper focuses on temporal lobe epilepsy (TLE), which is the most frequent form of partial epilepsy in adults [6].

Anti-epileptic drugs (AED’s) are the primary treatment for epilepsy; however, medication is ineffective in up to 30% of patients [7]. For some of these individuals, surgery can be an effective treatment option [8, 9]. Epilepsy surgery is extremely successful in the control of seizures in focal epilepsies [10]. However, there are risks associated with surgery, including the possibility of memory decline, visual

impairment, aphasia, motor deficits and sensory deficits [11, 9]. Potential risks to behaviour and cognition are assessed pre and post-surgery by specialists in the field of epilepsy, including clinical neuropsychologists. Assessment of language laterality and the impact of surgery are predicted using various standardised measures and medical procedures [12].

1.1.1. Temporal lobe epilepsy

Temporal lobe epilepsy (TLE) is a type of focal epilepsy that is characterised by recurrent, unprovoked seizures originating in the medial or lateral temporal lobe [4]. TLE can be associated with medial temporal sclerosis [14], and other structural abnormalities within the temporal lobes. In TLE, memory abilities can be reduced when mesiotemporal and associated neocortical structures are affected by lesions, due to on-going epileptic activity, or as a side effect of surgical treatment [14]. Treatment for epilepsy presents various challenges and surgery is a viable option in the treatment of TLE [15]. The primary goal of surgery is complete and continuous seizure cessation, however the impact on the patient's quality of life must also be ascertained [16]. Behavioural changes, for example, lack of independence as a result of role adjustment and cognitive changes such as memory and language problems have been reported as a consequence of surgery [17]. TLE patients with fewer abnormalities or without hippocampal atrophy on magnetic resonance imaging (MRI) are reported to have poorer memory outcomes following surgery [18], compared with those with greater abnormalities [19]. These findings are consistent with the known functions of the anterior temporal lobe (ATL) which encloses the hippocampus and medial structures that play a role in memory encoding. The potential for resection of these structures to pose a risk to cognitive functioning is therefore high [20]. Although temporal lobectomy is an effective treatment for medication resistant epilepsy patients, the risk of cognitive decline is high. Patients considering surgery must be fully informed of the potential risks involved [21]. This includes risk to episodic memory (EM) and semantic memory (SM). Episodic memory (EM) is defined as our memory for personal events in time; it is normally accompanied by remembering, for example, what happened, where and when [22]. Examples of EM include I have an appointment

tomorrow at 9am with the dentist or during a cognitive assessment how many words are recalled after hearing a list of words. Semantic memory (SM) is the memory necessary for the use of language; it is not dependent on how or when this knowledge was acquired [22]. It represents organised knowledge about words and other verbal symbols, concepts and relations. An example of SM would be that a Labrador is a type of domesticated animal called a dog, which barks and has four legs. Overall, SM is the part of long term memory which represents knowledge of objects, facts, and concepts and their inter-relationship [22, 23].

1.1.2. Impact of TLE surgery

The consequences of epilepsy surgery have long been documented, such as the case of H.M. who developed a dense amnesia following bilateral temporal lobe resection, which resulted in impaired capacity for learning new material, and recalling events after a delay [24]. Such studies have been instrumental in providing a strong evidence base for the underlying role of the hippocampal structures in memory [25]. The hippocampus is implicated in the formation of all aspects of conscious memory, including EM and SM. Post-operative amnesia following unilateral temporal lobectomy is well documented in the literature [26, 27, 28] and surgery may pose more risks to memory than other treatments for epilepsy [29]. Memory impairments in this population are often described as unilateral and material-specific, i.e. verbal or visual depending on lateralising factors for the individual [30]. Current research suggests that left TLE surgery is associated with a decline in learning and retention of verbal material, and right or non-dominant hemisphere surgery with a decline in non-verbal memory, although this is not unequivocal [31]. Some studies evaluating general intelligence post-surgery have reported no decline [32,33], whereas other studies have reported improvement in memory and IQ after TLE resection [34]. Language and comprehension difficulties are not frequently reported after dominant temporal lobectomy however subtle deficits in naming are common [35]. These word finding difficulties are more typically seen following a dominant temporal lobe resection and can persist 12 months post-surgery [28]. Despite this, patients do not usually spontaneously complain about their word finding difficulties [21]. Generally, SM

impairments are reported less consistently than EM [36] and some findings suggest that SM is intact subsequent to surgical resection [37, 38, 39]. However, a more recent study utilising sensitive measures of SM [40] found this to be compromised post surgically [41]. Conflicting findings in the literature may relate to the variability in neuropsychological measures used [31], or other factors, as discussed below.

1.1.3. Possible explanations for the inconsistency of findings regarding SM

The key role of assessment in epilepsy surgery candidates is to assess language functions and hippocampal integrity to sustain memory as essential language areas may be situated within the borders of the typical anterior temporal lobe [42]. Classical cognitive assessment includes exploring functions such as memory, problem solving, attention, concentration, and language function. Pre-and-post-surgical patients often complain of EM problems, and SM difficulties such as language disorders are rarely reported. However, anomia and verbal fluency impairments may be present in dominant left TLE surgery [43]. There may be a number of reasons why post-surgical reports of SM impairments in the literature are rare; formal assessment may be lacking, or loss of general knowledge, non-episodic information, and conceptual difficulties may be under played by the patient as they are not vital to their everyday functioning. These factors may lead to a tendency to focus on EM difficulties [44]. This suggests that if these aspects of cognition and memory are not formally assessed, they may be overlooked. This is of ethical importance because neuropsychologists preparing patients for surgery are required to fully inform the patient and team of the potential impact on memory and language. Subjective memory complaints often do not match objective memory findings in this group [45]), which suggests that patients may lack insight into their cognitive difficulties [46]. For example, Fargo et al., (2004) [47] found that epilepsy patients were more likely to accurately rate their memory function, but overestimate their language and attention abilities. It may be that patients do not possess the neuropsychological language to label their memory difficulties, highlighting a clinical challenge.

Poor self-reported neurocognitive functioning has been related to anxiety and depression and poor adjustment [47,45]. It has also been suggested that anxiety and depression may distort the reporting of everyday memory difficulties [48], and that memory complaints may be a reflection of adjustment and coping rather than memory impairment per se [45]. One possibility is that tests of SM are not viewed as a priority, as assessment is usually focused on EM [27, 49, 50]. This is also evident in the literature comparing self-report and objective measures in this population which has focused on EM [45]. However, few studies have formally tested for SM using a self-report measure. It is also possible that patients are less likely to report difficulties which do not affect them greatly on a daily basis. This is important to investigate, as it is possible that there is greater change in neurocognitive function and subsequently in quality of life than is predicted solely on the basis of standard testing. The current study therefore aimed to determine whether assessing SM via self-report (subjective assessment) would correspond with neuropsychological assessment of SM (objective assessment) findings.

1.1.4. Aim

The aims of this study were to investigate the following in a sample of TLE resection patients:

1. Compare subjective (self-reported) and objective (tailored neuropsychological assessment) measures of SM.
2. Explore differences between left and right TLE patients' self-report data.
3. Identify key factors affecting post-surgery quality of life using qualitative methodology.

1.1.5. Hypothesis: SM deficits will be apparent across both objective and subjective measures.

1.2. Method

1.2.1. Design

The project was funded by the Medical Research Council (MRC). Part funding was also provided by a small grant from Epilepsy Action. This paper is the second paper; the first paper provided theoretical insights into SM in this population (see [41]). This study received ethical approval from the Multicentre Research Ethics Committee (MREC). Research and Development approval was not required (Appendix 2F).

1.2.2. Participants

Participants consisted of a retrospective series of 20 TLE patients (11 female, nine male) with a broad age range (mean 36, min= 24, max= 55) who underwent standard anterior temporal resection (nine left and 11 right) to treat their epilepsy. They were recruited from a NHS specialist neuroscience centre in the UK [41]. The selection process involved searching through a clinical database of epilepsy surgery records to identify suitable post-surgery candidates. All patients had standard 'en bloc' resection for difficult-to-treat or medically refractory focal epilepsy. Patients were thought to be in the post-acute phase at testing (months post-surgery: mean = 35, range = 8 - 84, SD = 19.9) and had long-standing epilepsy (age of diagnosis, years): mean = 13.1, range = 4-45, SD = 10.1). Volume of resected (cm^3) temporal lobe tissue was estimated from the histopathology information (mean = 31.9, range = 0.144-92.0, SD= 24.2).

The recruitment process was exhaustive and all possible cases were explored. Patients with epilepsy associated with other neurological disease e.g. head injury, stroke, glioma and patients with psychiatric history and developmental disorders were excluded. All participants gave informed consent to participate in the study. Background characteristics of the sample are provided in Table 1. Pre-surgical measures of anxiety and depression (The Hospital Anxiety and Depression Scale, HADS [51]) were available for 75% of the sample.

1.2.3. Materials

1.2.4. Subjective measures of neuropsychological functioning

A brief questionnaire was constructed in accordance with the study aims (Appendix 2A). This measure was devised to evaluate the main aspects of SM and areas of clinical interest. The questions were selected for their clinical relevance in epilepsy and their theoretical interest.

Neuropsychologists working in the area of epilepsy surgery were consulted to assist with phrasing the questions in a patient-friendly way. The questionnaire included six questions:

1. *Have you had any problems remembering things?* This question provided the participant the opportunity to describe any memory problems experienced, which may include impaired personal EM [52]. Three of the questions focused on comprehension of general knowledge or conceptual knowledge whilst reading, during conversations or naming [53]:
2. *Have you experienced any problems with understanding conversation?*
3. *Do you have any problems recognising or naming objects?*
4. *Have you had any problem with understanding written information?*
5. *Have you experienced any problems with your mood or behaviour?* A general question pertaining to mood and behaviour problems was also included.
6. *Have you experienced any other problems since the surgery?* This final question provided the individual the opportunity to report any other problems they may have experienced since surgery.

The questions were selected by neuropsychologists, and were considered to correspond with the objective measures of SM employed. The administration of the questionnaire consisted of two phases: six questions enabling a semi structured interview and an opportunity for the individual to rate perceived severity of their problems on a 10 -point Likert scale (Appendix 2A) ranging from ‘never’ to ‘always’.

1.2.5. Procedure

Participants were contacted via telephone and letter (Appendix 2H) and invited to take part in the study. They were visited in their homes and consenting participants (Appendix 2I) were assessed over one or two, two-hour testing sessions. Demographic information and medical history were collected by reviewing medical notes and self-report during a clinical interview. Participants were administered a neuropsychological battery (objective assessment) and a questionnaire (subjective assessment).

1.2.6. Data analysis

A Kendall's Tau b, correlation analysis between subjective (questionnaire) and objective (standard neuropsychological tests) measures was used. Quantitative content analysis was also used to systematically evaluate participants' self-report to six questions from the questionnaire (Appendix 2A). Participants' responses to the six questions were coded and explored for emerging themes relating to quality of life (QOL). The differences between self-report of SM problems for patients with left or right sided temporal lobe surgery were explored [54].

1.2.7 Coding of content categories

In order to discover the type of cognitive problems reported, each of the patient's responses was coded for three categories (EM, SM, other). The SM category was expanded further to explore aspects of SM (naming, word finding difficulties, comprehension). The category system was driven by the research questions and emerging themes [54]. Looking through the data for each patient, the categories were coded for the presence or absence of that concept. This data was split according to each patients 'surgical side (left or right); and is represented as a percentage of the self-reported difficulty being present or absent in Table 5. The accuracy of coding was confirmed by an independent person, who rated a subset (10) of the questionnaires (five left and five right). An overall mean agreement rate of 95% was achieved on the six categories.

1.2.8. Table 1: Sample characteristics

Patient no.	Age	Months post-surgery	Education (Years)	Language dominance (WADA)	Occupation	Age at Diagnosis (Years)	Pre surgery HADS score		MRI	Pre-surgery Seizure Frequency
Left TLE resection				**-**			**Anx**	**Dep**		
1	24	21	21	-	University student	7	-	-	-	Weekly
2	49	17	18	-	Senior operations manager	45	9*	8*	Cavernoma	Biannually
3	30	24	18	-	Accounts assistant	15	8*	4	-	Weekly
4	25	17	21	-	Volunteer	15	8*	4	Bilateral small hippocampi	Daily
5	28	8	16	-	Packer	15	5	3	-	Weekly
6	32	60	18	Left	_	15	13*	5	Reduced left hippocampal volume and high T2 signal	Daily
7	46	60	16		Machinist	22	1	2	Reduced left hippocampal volume	Weekly
8	38	30	16	Left	Shop assistant	5	10*	4	Reduced left hippocampal volume	Monthly
9	32	36	18	Left	Accounts assistant	13	7	4	Left hippocampal atrophy	Weekly

Right TLE resection										
10	24	48	22	Left	Youth worker	10	1	2	-	Daily
11	55	36	21		Accountant	5	-	-	-	Monthly
12	32	36	21	Left	IT analyst	16	11*	8*	Reduced right hippocampal volume	Daily
13	27	74	16	Left	Distribution centre assistant	19	-	-	-	Weekly
14	39	17	18	Left	Butcher	4	-	-	Right hippocampal atrophy	Daily
15	49	84	16	Left	Store Keeper	7	14*	6	Hippocampal atrophy	Daily
16	21	36	16	-	Shop Manager	8	-	-	Right hippocampal atrophy	Weekly
17	42	17	18	Bilateral	Mail line operator	17	15*	7	Right hippocampus foreign tissue lesion	Daily
18	43	48	16	-	Lab technician	6	18*	11*	Hippocampal asymmetry (right<left)	Weekly
19	28	36	21	Left	University student	4	9*	1	Reduced right hippocampal volume	Daily
20	32	41	16	Left	Nursing assistant	10	5	19*	Hippocampal asymmetry (right<left);hippocampal abnormalities bilaterally	Weekly

Note:* Score < 8 on either the Anxiety or Depression subscale of the Hospital Anxiety and Depression Scale; Education years = age when leaving formal education.

1.3. Neuropsychological assessment

1.3.1 Objective measures of neuropsychological functioning

Neuropsychological tests of general cognitive ability, memory and more selective tests of SM were administered [55] (Table 3). The scores obtained on background tests (Table 2) demonstrated a typical TLE sample (see 1.1.2). This study aimed to explore tests corresponding with the self-report measure (Table 3) which are the main focus of this paper.

Test material included tests from The Camden Memory Test (CMT) [56], which consists of two short recognition memory tests for verbal (words) and non-verbal (faces) stimuli. Adequate reliability has been demonstrated (Cronbach alpha; α = .86 for words and α = .77 for faces) for the CMT [56]. There are 15 faces or words in each test and the total score is out of 15. The digit-span subtest (WAIS IV) was administered; adequate reliability has been demonstrated (Cronbach alpha α = .0.90) [64]. The longest number of digits a person can repeat back is noted, for both forward and backward repetition. The Rey-Osterrieth Complex figure was administered; adequate reliability has been demonstrated (Cronbach alpha; copy or learning α = .0.79 and recall α = .0.77) [65]. For this test the individual makes an exact copy of a complex figure which is then removed and they are requested to replicate this from memory. The Raven's Coloured Progressive Matrices test was also administered, for which adequate reliability has been demonstrated (Cronbach alpha; α = .90) [66]. This was delivered using a booklet, it is a nonverbal test made up of 60 stimuli; the individual is asked to select which drawing best fits into a matrix, administered in order of difficulty.

The semantic tasks were taken from a battery of tests that have been used to assess SM impairment in other clinical patient groups [40, 55]. The 96–trial Synonym Judgement Test requires the participant to match a target item with one of three options presented in written and spoken forms. It has been demonstrated to be a sensitive measure both clinically [40, 55] and in research using repetitive transcranial magnetic stimulation (rTMS) [57, 58] and fMRI studies [59]. This test has 96 trials and it was employed in its timed form; no reliability data is available for this measure. The 64 Naming Test from The Cambridge Semantic Battery [60],

which consists of 64 line drawings of everyday objects and animals, was administered [61]. No reliability data is available for this measure. The test was presented in paper form and both test accuracy and speed were recorded. The Graded Naming Test (GNT) [62], which consists of 30 psychometrically graded line drawings of objects that the patient is required to name, was also administered. Adequate reliability has been demonstrated for the GNT (Cronbach alpha; α = .0.92) [62].

1.3.2. Measure of emotional status

The HADS is a brief (14-item), widely used self-report measure of anxiety and depression [51]. Raw scores for both Anxiety and Depression sub-scales, can be categorised into mild (8-10), moderate (11-15) and severe (16 or above) cases [63].

1.3.3. Controls

Test performance of patients was compared against a control group [41]. The control group selected was thought to be conservative (Appendix 2J). A matched control group was thought to be unfeasible given the variability in sample characteristics (Table 1).

1.3.4. Table 2: Objective test results

Neuropsychological Test	**Max. score**	**Mean**	**Cut-off**	**Left TLE**	**Patient No.**								**Right TLE**	**Patient No.**								
General test				1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Camden Recognition memory																						
Words (percentile)	-	-	-	**5**	**5**	**<5**	**5**	**5**	**<5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	25	**5**	**5**	**5**	**5**	**5**	**5**
Faces (percentile)	-	-	-	90	20	75	90	50	75	75	75	75	75	90	50	90	25	**5**	50	90	50	75	50
Digit span: forwards	-	6.8	5	5	**4**	7	6	6	5	6	**4**	5	6	6	8	7	5	6	6	7	**3**	5	7
Digit span: Backwards	-	4.7	2.3	4	4	5	5	6	3	5	3	**2**	5	4	6	3	3	4	4	4	**2**	**2**	3
Rey figure copy	36	31.03	31	36	31	31	34	34	33	35	36	**30**	36	**26**	36	36	33	**23**	34	31	33	36	34
Rey Immediate recall	36	18.3	9	24	19	**5**	17	17	18	17	17	12	31	15	21	24	17	9	23	23.5	12	16	**1.5**
RCPM (percentile)	-	-	-	95	95	90	95	95	95	90	95	95	95	95	95	95	90	50	95	90	95	90	75
Semantic Memory tests																							
Graded Naming test (GNT)	30	22.1	13.5	16	17	14	**13**	**13**	**10**	14	**13**	**7**	16	26	22	19	21	17	21	15	16	**13**	14
64 naming test	64	62.3	59.1	62	60	**59**	63	61	**59**	60	64	**53**	62	62	63	64	62	61	61	63	63	61	60
Synonym judgement	96	94.4	92.05	**86**	**84**	**84**	**83**	**80**	**78**	**74**	**71**	**69**	**90**	**90**	**88**	**88**	**88**	**87**	**87**	**86**	**81**	**79**	**75**

Note: bold text = below cut-off performance.

1.3.5. Table 3: Objective test purpose and utilisation in comparison with subjective questions

Tests (Objective)	Measured neurocognitive function	Background characteristic	Utilised in analysis	Corresponding questionnaire question/No. (Subjective)
Digit span (WAIS IV) [64]	STM/Working memory	✓		N/A
Rey-Osterrieth Complex Figure [65]	Visuospatial constructional ability and visual memory	✓		N/A
Raven's Coloured Progressive Matrices [66]	Non-verbal test of intellectual ability	✓		N/A
Camden Recognition Memory Test [56]	Recognition memory test for words and faces	✓	✓	1.Problems remembering
Graded Naming Test [62]	Object naming ability (language)	✓	✓	2. Problems understanding conversations 3.Recognising objects 5. Understanding written information
Cambridge 64 Naming Test [60]	Object naming ability (language) timed version	✓	✓	2. Problems understanding conversations 3.Recognising objects 5. Understanding written information

96 Synonym Judgement test [55]	Semantic processing (timed version)	✓	✓	2. Problems understanding conversations 3.Recognising objects 5. Understanding written information

1.4. Results

A brief summary taken from the earlier paper [41] is provided in Table 2. In summary, the background neuropsychology testing data highlighted that the sample selected was representative of the TLE post-surgery population as informed by the literature (see 1.1.3). Most participants scored in the impaired range on The Camden Memory Test (CMT), demonstrating anterograde amnesia for word recognition but not for unfamiliar faces. One participant with right temporal lobe (RTL) surgery was amnesic for both, and another one was at least low average on both tests. Seventeen out of 20 participants demonstrated performance above the control cut-off on digit span forwards and backwards. Seventeen out of 20 participants demonstrated no difficulties with visuospatial constructional abilities as measured by the Rey Figure Copy and 18 out of 20 on immediate visual recall. All participants demonstrated performance in the average range and above on the Raven's Coloured Progressive Matrices. In comparison with control data, performance on the semantic tasks was as follows: on the 64 Naming Test, three out of nine left TLE (LTLE) resection patients under performed. Graded naming test scores were worse for the LTLE resection patients (5 out of 9 abnormal scores); all but one of the RTLE patients demonstrated no difficulties. All participants' scores were below control scores on the 96 Synonym Judgement Test and decision time (4.6 sec) was over twice that of controls (1.99 sec).

1.4.1 Emotional status

In a non-clinical adult population the mean Anxiety score was 6.14 (SD =3.76) and the mean Depression score was 3.68 (SD = 3.07) (Crawford et al., 2001). In the current sample, the mean Anxiety score was 9.23 (SD = 4.54, median = 9) and the mean Depression score was 7.00 (SD = 4.61, median = 6). Using a standard equation for calculating one sample z scores (z score = sample mean-population mean/standard error of the mean) the sample z scores on Anxiety (z= 2.97, $p>0.005$) and Depression (z= 3.90, $p>0.005$), reflected significantly high levels as a group, as compared to a normal population.

1.4.2 Correlational analysis

All analyses were completed using IBM Statistical Package for the Social Sciences software (SPSS) version 19.

This study aimed to determine whether participants' objective scores as measured by neuropsychological testing correlated with their self-reported difficulties. The self-report questionnaire provided continuous ordinal level data. The normality of the distribution was checked using histograms and measures of central tendency, skewness and kurtosis were also noted (Appendix 2B). Statistical tests of normality were also used to explore the distribution under investigation (Appendix 2B). Boxplots were created to identify univariate or multivariate outlier cases. Visual review suggested some non-normality; the mean, mode, median were dissimilar, skewness was apparent for some measures, and statistical tests of normality demonstrated some statistical significance. It was concluded that the data were not normally distributed, and also given the small sample size, nonparametric tests were considered appropriate [67].

Scatter plots were produced between the variables of interest and assumptions for running correlations checked (Appendix 2C). The data was checked for bivariate outliers and linearity [68]. Any extreme data points were checked by carrying out a sensitivity analysis to check for the extent of the outlier's influence. No influence was noted and the outliers remained in the final analysis. The data were analysed using a correlational design to ascertain the degree to which individuals or cases with high rankings on one variable were observed to have similar rankings on another variable. The correlations were calculated using Kendall's tau b, a rank correlation measure. This provides a good estimate of the value that would have been expected in the population and the approximation is accurate for smaller sample sizes [69]. Correlations were calculated using a two tailed test between the self-report measure and the standard neuropsychological tests; results are presented in a correlation matrix (Table 4) and discussed below.

1.4.3. Table 4: Correlation matrix

Kendall Tau _b

Correlations between the 5 subjective questions on semantic memory (SM), mood and 7 objective measures of SM	**1).** Remembering	**2).** Understanding conversations	**3).** Recognising objects	**4).** Mood & behaviour	**5).** Understanding written information	GNT	64 Naming (accuracy)	64 Naming (speed)	96 Synonym (accuracy)	96 Synonym (speed)	CMT (Words)	CMT (Faces)
1). Remembering	1	.457*	.464*	-.165	.392	.059	.200	.253	.084	.158	-.020	-.206
2). Understanding conversations		1	.338	.134	.829**	.132	.422*	.027	-.014	.013	.120	-.150
3). Recognising objects			1	-.232	.372	.092	.280	-.008	0.16	-.089	-.265	-.172
4). Mood & behaviour				1	.050	.043	.317	-.103	-.064	-.176	.285	.126
5). Understanding written information					1	.043	.352	.007	-.099	-.007	-.015	-.094
GNT						1	.006	-.459**	.704**	-.334*	.186	-.185
64 Naming (accuracy)							1	.028	-.187	.017	-.218	-.187
64 Naming (speed)								1	-.355*	.470**	.073	-.095
96 Synonym (accuracy)									1	-.350*	.194	.001
96 Synonym (speed)										1	.101	-.279
CMT (Words)											1	.038
CMT (Faces)												1

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

Note: Sample size: = 20
Graded Naming Test (GNT); Camden Memory Test (CMT)

1.4.4. Results of correlational analyses

No significant correlations were observed between the CMT and any of the subjective ratings or any of the other objective tests. The results of the SM measures were as follows: naming accuracy on The Cambridge 64 Naming Test was significantly correlated with the 'problems understanding conversations' question ($r = .422$, $n = 20$, $p = .024$). Naming speed on this test was significantly correlated with the GNT ($r = -.459$, $n = 20$, $p = .006$) and both accuracy ($r = -.355$, $n = 20$, $p = .031$) and speed ($r = .470$, $n = 20$, $p = .004$) on The 96 Synonym Judgement Test.

The GNT was not significantly correlated to any of the subjective ratings. GNT was significantly correlated with speed on The Cambridge 64 Naming Test ($r = -.459$, $n = 20$, $p = .006$), and both accuracy ($r = .704$, $n = 20$, $p = .000$) and speed ($r = -.334$, $n = 20$, $p = .046$) on The 96 Synonym Judgement task. Performance speed on The 96 Synonym Judgement task was not significantly correlated with any of the subjective ratings. Along with the above inter-measure correlations, accuracy was significantly correlated with the speed ($r = -.350$, $n = 20$, $p = .034$) on this test.

There were significant correlations between some of the self-report questions. The 'problems remembering' question was significantly correlated with the 'problems understanding conversations' question ($r = .457$, $n = 20$, $p = .023$) and the 'problems with recognising objects' question ($r = .464$, $n = 20$, $p = .026$). The problems 'understanding conversations' was significantly correlated with the 'problems understanding written information' question ($r = .829$, $n = 20$, $p = .000$). Pre-surgical scores on the HADS for depression but not anxiety were significantly correlated to self-report of mood difficulties ($p<0.05$, $r=.552$).

1.4.5. Effect size and correlation

The likelihood of type II errors can increase with a small sample size [68]. Therefore, it is recommended that a minimum level of power to aim for is .8, thus reducing the probability of making a type II error to .2 [68]. Correlation coefficients

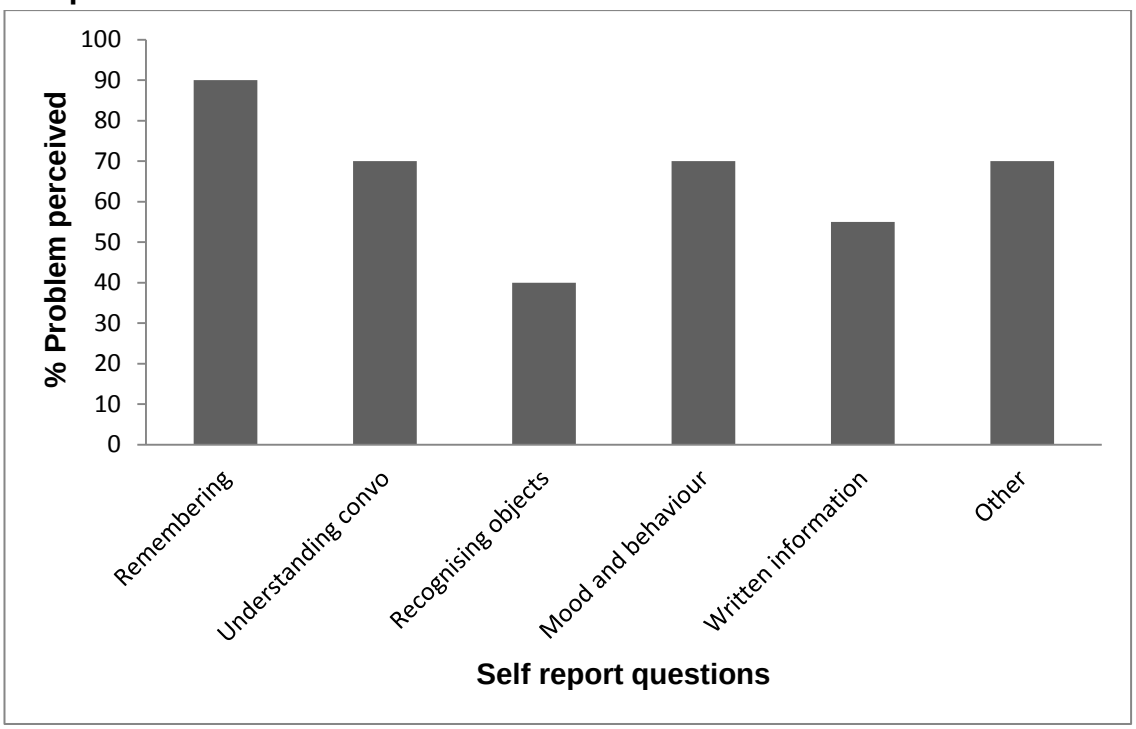
obtained can be observed to give an estimate of effect size (ES) [70]. According to Cohen (1988) [70], r=.1 constitutes a small ES, r=.3 is a medium ES and r=.5 is a large ES.

The ‘problems remembering’ question was approaching a medium ES with naming accuracy and speed (64 Naming Test) and CMT faces. The ‘problems recognising objects’ question reached a medium ES with naming accuracy (64 Naming Test) and CMT words. Nonetheless, these do not achieve the level which would indicate good convergent validity. A statistical power calculation adjusting for Kendall Tau-b was calculated for a given effect size, an estimation of sample size to achieve this was calculated. In order to achieve adequate power of .80 for a correlation with a medium effect size (r=.3), a two-tailed test and an alpha-level of .05, a sample size of 94 would be necessary.

1.5 Results of self-report analysis

An exploratory analysis was carried out on the self-report data available using content analysis. Berelson (1952) [71], defined content analysis as “a research technique for the objective, systematic and quantitative description of the manifest content of communication”. This methodology can be used with a range of data including micro level data [72]. Content analysis enables the researcher to measure the frequency of different categories and themes in the data. The unit of analysis was defined as text from the questionnaires. A coding scheme using a predefined set of concepts based on the six questions from the questionnaire was used [54]. Twenty people completed the self-report questionnaire and their responses within each category were counted (Fig. 1). Eighteen (90%) of the participants reported problems remembering, 14 (70%) reported problems with understanding conversations, 14 (70%) with mood and/or behaviour, 11 (55%) had problems understanding written information, 14 (70%) recorded a difficulty in the ‘other’ category and eight (40%) reported problems with recognising objects. The ‘other’ category was further explored for quality of life themes.

1.5.1 Figure 1. Histogram showing group % of self-reported difficulty for the six questions



1.5.2 Table 5: Percentage of perceived problem for each content category

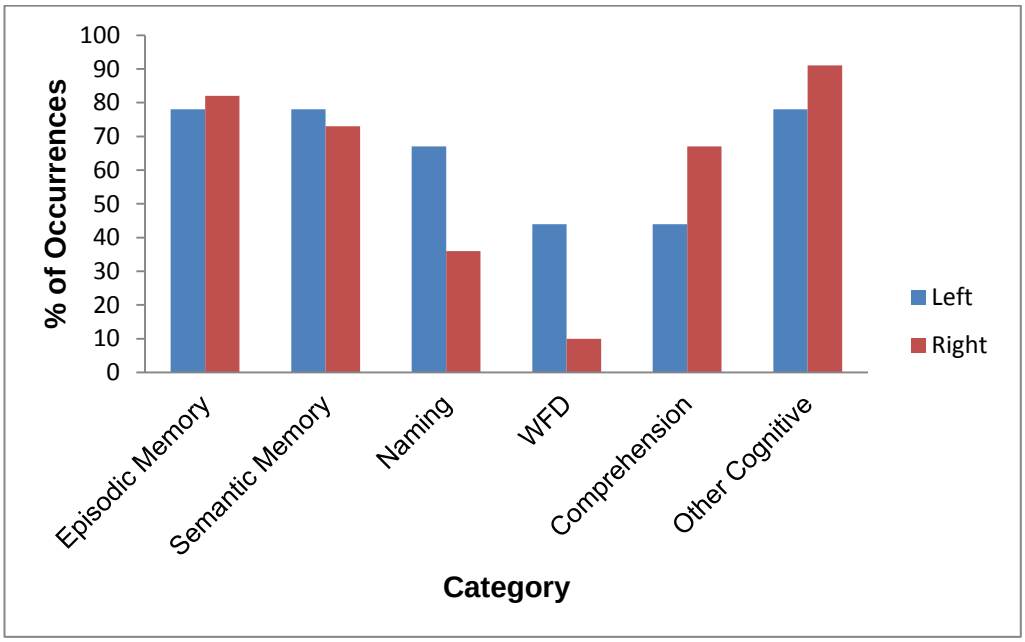
Category	Label	Description	LTL present %	LTL absent %	RTL present %	RTL absent %
1	Episodic memory [22, 23]	References to memory difficulties in remembering tasks, temporal related events	78	22	82	18
2	Semantic memory [22, 23]	References to language difficulties e.g. word finding, naming, comprehension	78	22	73	27
2a.	Naming	References to naming difficulties e.g. objects	67	33	36	64
2b.	Word finding difficulties (WFD)	References to WFD e.g. during conversation	44	56	10	90
2c.	Comprehension	References to comprehension difficulties e.g. difficulty in understanding written or spoken form of language	44	56	67	33
3	Other cognitive difficulties	References to processing speed, attention, concentration e.g. slowed down, doing two things	78	22	91	9

Note: LTL (left temporal lobe); RTL (right temporal lobe)

1.5.3 Quantitative content analysis

Figure 2 highlights the frequency of reports in the explored categories for patients with left and right surgery.

1.5.4 Figure 2. Histogram of the % occurrences of category difficulties by participants who have undergone left and right temporal lobe surgery



Chi square exact probabilities are reported (Table 6). The percentage of participants that experienced EM ($\chi 2 = 0.51$, $p = 0.82$, Cramer's V =.050) difficulties and SM ($\chi 2 = 0.67$, $p = 0.79$, Cramer's V =.058) difficulties did not differ statistically by surgical side; the effect size value did not meet Cohen's minimum standard (≥ .20) to be called a small effect size. Semantic memory was further broken down into naming ($\chi 2 = 1.82$, $p = 0.178$, Cramer's V =.302), word finding difficulties (WFD) ($\chi 2 = 3.30$, $p = 0.69$, Cramer's V =.406) and comprehension difficulties ($\chi 2 = 0.202$, $p = 0.653$, Cramer's V =.101). Reports of naming difficulties did not differ by surgical side, a medium effect size (Cramer's V =.302) was noted. WFD did not differ by surgical side; a medium effect size (Cramer's V =.406) was noted. There was no statistical difference in reports of comprehension difficulties by surgical side, a small effect size (Cramer's V =.101) was noted. Cognitive difficulties were also explored by surgical side ($\chi 2 = 0.669$, $p = 0.413$, Cramer's V =.183). There was no statistical difference in reports of cognitive difficulties, by surgical side; a small effect size (Cramer's V =.183) was noted.

1.5.5 Table 6: Results of Chi-square test & Cramer's V for category reports by surgery side

	Surgical side				
Category	*Left*	*Right*	*χ2*	*p*	*Cramer's V*
SM	7/9 (78)	9/11 (82)	0.67	.79	.058
EM	7/9 (78)	8/11 (73)	0.51	.82	.050
Naming	6/9 (67)	4/11 (36)	1.82	.178	.302
WFD	4/9 (44)	1/11 (10)	3.30	.069	.406
Comprehension	4/9 (44)	6/11 (67)	.202	.653	.101
Other cognitive	7/9 (78)	10/11 (91)	.669	.413	.183

Note: N=20, df = 1. Numbers in parentheses indicate percentages.
*p < .05

1.5.6. Qualitative content analysis

Content analysis of participant transcripts identified quality of life issues other than memory and cognition, relating to epilepsy surgery. Table 7 outlines the key five themes which outline the issues spontaneously expressed by patients, along with quotes used to illustrate themes. A range of issues were raised, broadly categorised under surgery outcome, adjustment and psychological issues. Some of the descriptions highlight a negative evaluation and others a positive. Emotional issues (65%) and adjustment issues (55%) predominated; psychological issues seemed to reflect reports of depression more than anxiety. Other issues reported by patients included identity and perception difficulties (40%) and post-operative concerns (20%). Patients also reported positive benefits as measured by accomplishments (40%).

1.5.7. Table 7: Themes based on content analysis of all participant transcripts

Theme	Description	N (%)	Patient (P) Quote
Identity & perception (seizures as part of life or not post-surgery)	Perceived success, pleased underwent surgery	5 (25)	P9: ”No seizures, huge difference to my life since surgery”
	Perceived failure	2(10)	P19: “Aura’s still present this is frustrating, after going through surgery”
	Loss of identity or missing seizures	1(5)	P20: “Although I don’t have fits anymore, I still miss them, I feel as though a part of me is missing”
Post-operative issues (acknowledging resultant other issues post-surgery)	Coping with other difficulties post-surgery including physical	4 (20)	P11: “I have had difficulty sleeping since the surgery” P19: “I suffer a lot with headaches if it is too cold or too hot, the weather affects the side of my head”
Adjustment & social stigma (impact on work or social life, social support, perceived stigma and low confidence)	Experience of on-going difficulties impacting on life; coping with on-going issues to do with others and own adjustment	11 (55)	P10: “Had to leave work due to memory problems” P20: “I find it hard to mix with a group of people”

			P19: “I hate the ignorance of the general public not understanding the condition”
Emotional difficulties (mood issues that are causing an impact on quality of life)	Psychological issues including depression, anxiety, anger, stress, frustration	13 (65)	P2:”Feel frustrated” P4:”I can be moody” P6:”Snap very easily get angry and irritable” P10: “Feel very depressed” P17:”I find I sometimes worry too much”
Positive benefit in quality of life e.g. memory/mood/confidence/work education (goal achievement since surgery, positive impact on quality of life)	Self-monitoring of success, gains/accomplishment since surgery	8 (40)	P1:”My mood is better since the surgery” P9: “I have taken further education and been promoted on two occasions” P9: “My memory is much better since the surgery”

1.6. Discussion

1.6.1 Summary of aims & key findings

This study aimed to add to the limited evidence base regarding SM impairments in patients who have undergone unilateral resection for TLE. It is the first study to evaluate SM using both subjective (self-report) and objective measures (neuropsychological test performance) by utilising a tailored assessment. The results from this study indicate that, in general, self-report ratings of SM are not significantly correlated with objective neuropsychological testing in a sample of post-surgical TLE patients. This finding replicates findings from previous studies that highlight discrepancies between these two forms of evaluation [73, 74]. The only significant finding with respect to self-report and neuropsychological tests was between self-reported problems with 'understanding conversations' and The 64-Naming Test, taken from the Cambridge Semantic Battery [60]. The amount of variance accounted for between naming test accuracy and self-report reached a large effect size. The results of the between group content analysis comparisons, reached a medium effect size for both naming and word finding difficulties. Left sided TLE surgery patients were more likely to report naming and word finding difficulties. These results are in parallel with performance on the graded naming test on which left surgery patients' performance was inferior as compared to right TLE. This finding is in line with the literature on difficulties experienced by patients with speech dominance in the left hemisphere [28]. They are also supportive of the role suggested for the left temporal neocortex in storing and retrieving semantic knowledge [89].

1.6.2 Possible explanations for the findings

If SM impairments were present, one may have expected to find deficits across modalities (i.e. in both naming and comprehension) and across both objective and subjective measures. However, this was not the case which requires further

explanation. One possibility is that the measures employed were not reliable, however, these measures of SM have been utilised in various patient groups and convergent validity was demonstrated in the current study (Table 4). It is also possible that non-significant relationships between subjective memory tests and objectively measured memory may represent under reporting of memory problems on the self-report measure. This could suggest that the observed non-significant relationship is due to factors such as sample size and statistical power. However, given the nature of epilepsy, it may also demonstrate that participants did not recall these difficulties due to problems with remembering or unawareness of cognitive impairment (anosognosia). There were some significant correlations between self-report questions, for example 'problems understanding' correlated with 'problems remembering'. This may indicate that when patients experience difficulties with understanding information, it is less likely to be remembered, or that some patients are more likely to report difficulties in more than one area. It may also purely reflect the difference between patients' and neuropsychologists' concepts of neuropsychological impairment. There were no correlations between the CMT and any self-report memory questions. It could be argued, therefore, that neuropsychological tests may not detect and correspond to the functional difficulties experienced on a daily basis by patients [75]. Exploration of patients' data revealed that eight or more participants reported difficulties across areas of self-report including SM and EM. This may suggest that patients are aware of their difficulties; however, it could be that they have difficulties with labelling or differentiating between SM and EM problems, as found by other studies (see [44]). This was further explored by content analysis of reports in EM and SM domains; no statistical difference within these categories was found between left and right TLE surgery patients. Further exploration of SM (Table 5) revealed no statistically significant difference in rates of self-report between left and right surgery patients. However, a medium effect size was noted for both naming and word finding difficulties. Left TLE surgery patients may report naming and word finding difficulties more commonly than right TLE surgery patients, which would be consistent with views on dominant temporal lobe resection and verbal memory deficits [28]. Some of these factors are further explored.

1.6.2 Naming as a measure of SM

Overall, SM impairments are not demonstrated on standard measures for participants in this study; with the exception of more challenging tests such as the Graded Naming Test and The 96 Synonym (Table 2). Naming tests are used in standard epilepsy surgery assessments; they are sensitive in providing insight into the quality of the underlying semantic system [76]. Both left and right TLE patients in this study reported naming and word finding difficulties, however, these were more prominent for left TLE surgery. In speech production, naming requires the ability to move from meaning to speech, and difficulties can be seen to represent a problem within the semantic system. The degree to which symptoms such as word finding difficulties are experienced, has been noted to be analogous to underlying brain pathology [77]. Distributed models of speech production suggest an arbitrary relationship between semantic level activation and subsequent phonological access required for speech. This is thought to be vulnerable to the level of activation received and under activation of the system may result in symptoms such as naming difficulties; furthermore, this can be improved by a prompt or feedback from the environment [78]. Perhaps surgery impacts the level of activation required within the semantic system. Comprehension abilities are less sensitive to semantic impairment than expressive tasks, and assessment of comprehension abilities needs to be enhanced by including a measure which consists of conditions such as low frequency and more abstract words and response timing [41]. This type of assessment method is more sensitive at detecting semantic impairment [40].

1.6.3 Clinical implications

In clinical practice it is important to consider the relevance of level of SM impairment to everyday life. Naming difficulties are more consistently reported than, for example, comprehension difficulties. It is possible that sensitive level of self-report on SM is reliant on feedback from the self or the environment (e.g. incorrect naming being pointed out during conversation). During speech, an individual may be more consistently exposed to feedback for naming difficulties,

via self-correction or environmental feedback. In contrast, comprehension skills may be less reliably exposed to feedback from the environment and therefore be at a lower level of awareness. In contrast, impaired performance on sensitive comprehension tests such as The 96 Synonyms (Table 2), demonstrates SM impairment. In daily life, individuals are less likely to be exposed to this level of manipulation (infrequent, abstract words etc.) reducing the possibility of feedback at a sensitive level from the environment. It seems unlikely that individuals with TLE resection are anosognosic or lacking in self-awareness, as based on this study they report a range of problems. However the degree of perceived impairment is perhaps analogous to the level of self-awareness, which is strengthened by feedback. It is possible that subtle SM impairments do not cause patients difficulties on a daily basis and therefore this may be less likely to be scored highly on a self-report measure. In addition, the nature of memory problems may mean that patients do not recall their difficulties, highlighting the importance of corroborating information from various sources in clinical practice, including with formal assessment and observations. The aim of surgery is seizure control; however, factors such as memory, adjustment, mood, social stigma can all have an impact on quality of life. Clinical psychologists working with this client group need to complete a holistic assessment as the risks faced by each patient are variable and can differ according to individual characteristics. For some the adjustment process can involve a slow transition from a sick role to normal life; if expectations of positive life are not met there can be disappointment [90]. A patient-centred approach with a focus beyond seizure control is essential. Further research exploring the benefits of therapy in this patient group is required; however, Cognitive behavioural therapy (CBT) is a useful intervention for treating depression and improving quality of life in patients with TLE [86].

1.6.5 Factors beyond memory

This exploration also demonstrated that both left and right TLE patients report slowed processing, concentration and attention difficulties. This is consistent with dysfunction associated with extra-temporal regions, and may reflect the

multifactorial nature of cognitive impairment [14]. Perception of memory problems can also be influenced by impairment of other cognitive functions, such as attention and concentration [79], anti-epileptic medication, clinical, and psychosocial factors [80].

Post-operative recovery does not seem to be limited to cognitive functioning; the qualitative analysis highlighted that 65% of the sample reported emotional issues and 55% reported adjustment issues post-surgery which may contribute to a reduced quality of life. Factors such as perception of seizure control seemed to play a crucial role in sense of identity (40%), as did post-surgery issues (20%). However, at least 40% reported a positive impact on QOL due to improvement in functioning at some level.

1.6.6 Mood and TLE surgery

The misperception of memory difficulties has been connected to mood problems [81]. Scores on pre-surgical measures of depression were significantly correlated with post-surgical self-report of mood difficulties; a large effect size was noted; however, pre and post anxiety scores were not related. This may indicate that participants experienced a reduction in anxiety due to better seizure control (as found by [82]), whereas depression persists and surgery has little impact on mood. Psychological factors including low mood have been reported to impact on cognitive functioning [83]. TLE patients are thought to be generally more vulnerable to depression for a multitude of reasons including temporal lobe pathology [84] and adjustment post-surgery [85]. There is a lack of data regarding treatment and management of patients with comorbid depression; one study highlights the utility of CBT [86], however post-surgery data is scarce. CBT is recommended by clinical practice guidelines [87] for treatment of depression, this requires further consideration in patients with epilepsy.

1.7 Limitations

There are a number of limitations to this study, as discussed below.

1.7.1 Use of non-validated measures

The questionnaire used in this study met the research objectives; however, it was not a validated measure. The questions selected adequately probed particular issues of interest, however without sufficient piloting it is difficult to be certain as to the concepts being measured. The questionnaire was worded to encourage complete information, however this was constructed via clinicians rather than patients. This study is a pilot of this tool and standardising it with control data or another patient population would be a useful area for future research and development.

1.7.2 Sample

The sample consisted only of post-surgical patients and a pre/post-surgery design would have enabled a broader discussion of memory problems pre and post-surgery. In addition, there was a marked variation between length of time post-surgery, which may potentially impact on cognitive performance and perception of this. Finally, the group size, while typical of similar studies in TLE surgery, was underpowered, thus limiting the power of any analysis.

1.8 Conclusions

1.8.1Clinical practice

The findings from this study suggest that SM may be assessed more accurately by utilising a tailored assessment approach. The results demonstrate that patients who experience a change in their memory abilities are not accurate at reporting post-surgical SM abilities, unless this is sensitively assessed using naming tests, sensitive receptive tests and tailored self-report. Adapting a tailored subjective/objective approach to assessment enhances the clinicians' ability to derive formulation and subsequent intervention. For example under reporting of difficulties with low scores on objective measures may require a cognitive rehabilitation of memory to raise awareness; whereas over reporting of difficulties and low scores on objective measures, may indicate mood problems requiring a therapeutic CBT based intervention. The questionnaire in this study adds to clinical utility and can be validated through clinical feedback. It is important that sensitive naming tests are available and utilised in clinical practice, and also that

they are ecologically valid [88]. This research also adds to existing literature in demonstrating that surgical intervention can be an effective treatment for seizure relief, however psychological needs may persist following surgery. Patients should be fully informed and adequately supported to aid their adjustment.

1.8.2 Overall conclusion

In conclusion, the present study adds to the body of research investigating self-report and objective measures in TLE resection patients. The results concur with the current literature in that there was a discrepancy between self-reported difficulties and those measured by standardised tests. The results support the idea that naming tests are good predictors of SM impairment. Sensitive measures and self-report may provide a further framework for understanding SM impairment in TLE. The need for adequate provision of psychological support, to aid adjustment and build on positive outcomes post-surgery is emphasised.

References

(1) MacDonald, B.K., Cockerell, O.C., Sander. J.W., & Shorvon, S.D. (2000). The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain*. 123,665-676.

(2) Clinical Standards Advisory Group.(2000). *Services for Patients with Epilepsy.* London: Department of Health.

(3) NICE The epilepsies: diagnosis and management of the epilepsies in adults and children in primary and secondary care. *National Institute for Clinical Excellence (NICE) Clinical Guideline*. January, 2012.

(4) Engel, J. Jr. (2001). A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia*. 42, 796-803

(5) Fisher, R.S., van Emde Boas W., Blume, W., Elger, C., Genton, P., Lee, P., & Engel, J., Jr. (2005) Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 46, 470-472.

(6) Semah, F., Picot, M.C., Adam, C., Broglin, D., Arzimanoglou, A., Bazin, B., Cavalcanti, D., & Baulac, M.(1998) Is the underlying cause of epilepsy a major prognostic factor for recurrence? *Neurology*. 51,1256–62.

(7) Kwan, P., & Brodie, M.J. (2000). “Early identification of refractory epilepsy,” *The New England Journal of Medicine.* 342, 314-319.

(8) Engel, J., Weibe, S., French, J., Sperling, M., Williamson, P., Spencer, D., Gumnit, R., Zahn, C., Westbrook, E. & Enos, B. (2003). Practice

parameter: temporal lobe and localized neocortical resections for epilepsy. *Epilepsi.* 44, 741-51.

(9) Spencer, S. & Huh, L. (2008). Outcomes of epilepsy surgery in adults and children. *Lancet Neurology*. 7, 525-537.

(10) Wiebe, S., Blume, W.T., Girvin, J.P., & Eliasziw, M. (2001). Effectiveness and efficiency of surgery for temporal lobe epilepsy study group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med.* 345,311-8.

(11) Martin, R.C., Sawrie, S.M., Roth, D.L., Gilliam, F.G., Faught, E., Morawetz, R.B., & Kuzniecky, R. (1998). Individual memory change after anterior temporal lobectomy: a base rate analysis using regression-based outcome methodology. *Epilepsia* 39:1075–82.

(12) Thompson P.J. (1997). Epilepsy and memory. In Cull CA, Goldstein LA (Ed.), *Clinical psychologists handbook of epilepsy: assessment and management* (pp. 35 - 53). Routledge. London & New York.

(13) Wiesser HG. (2004). Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis. *Epilepsia.*45, 695-714.

(14) Helmstaeder C. (2006). Cognitive Outcomes in Patients with Chronic Temporal Lobe Epilepsy*. Epilepsia.* 47(Supple2) 96–98.

(15) Wiebe S. & Jette, N. (2012). Epilepsy surgery utilization: who, when, where and why? *Curr Opin Neurol.* 25,187-193.

(16) Wiebe S. (2006) Outcome measures in intractable epilepsy. *Adv Neurol.* 97,11–5.

(17) Baxendale, S. (2008). The impact of epilepsy surgery on cognition and behaviour. *Epilepsy & Behaviour.* 12, 592-599.

(18) Hermann, B. P., Wyler, A. R., Somes, G., Dohan, F. C., & Clement,L. (1994). Declarative memory following anterior temporal lobectomy in humans. *Behavioral Neuroscience*, 108,3-10.

(19) Sidenberg, M., Hermann, B.,Wyler,A., Davies, K.,Dohan, C & Leveroni, C. (1998). *Neuropsychology.* 12, 303-316.

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

(21) Lee, G.P. (2010). Neuropsychology of Epilepsy and Epilepsy surgery. Oxford workshop series. *American academy of clinical neuropsychology*. Oxford University Press. pp.165181.

(22) Tulving, E. (1972). Episodic and semantic memory. In E. Tulving &. W. Donaldson (Eds.), *Organization of memory.* New York: Academic Press. pp.381-403.

(23) Tulving, E. (1983). *Elements of episodic memory.* New York: Oxford University press.

(24) Scoville, W.B. (1954).The limbic lobe in man. *J Neurosurg*. 11, 64–6.

(25) Penfield, W. & Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *Arch Neurol Psychiatry*. 79, 475–97.

(26) Walczak, T.S., Radtke, R.A., McNamara, J., Lewis, D., Luther, J.,Thompson, E., Wilson, W.P., Friedman, A.H., & Nashold, B.S. (1990). Anterior temporal lobectomy for complex partial seizures: evaluation, results, and long-term follow-up in 100 cases. *Neurology.* 40, 413-18.

(27) Jones-Gotman, M., Smith, M. L., & Zatorre, R. J. (1993). Neuropsychological testing for localization and lateralization of the epileptogenic region. In J. Engel Jr. (Ed.), *Surgical treatment for epilepsies*. New York: Raven Press, pp. 245–262.

(28) Langfitt, J.T., & Rausch, R. (1996). Word-finding deficits persist after left anterotemporal lobectomy. *Arch Neurol.* 53, 72–6.

(29) Helmstaedter, C., Kurthen, M., Lux, S., Reuber, M., & Elger, C.E. (2003). Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. *Ann Neurol.* 54, 425–32.

(30) Invik, R.J., Sharbrough, F.W., & Laws, E.R. (1987) Effects of anterior temporal lobectomy on cognitive function. *J Clin Psychol.* 43,128–37.

(31) Lee.T., Yip, J. & Jones-Gotman. M. (2002). Memory Deficits after Resection from Left or Right Anterior Temporal Lobe in Humans: A Meta-Analytic Review. *Epilepsia*. 43, 283-291.

(32) Keogan, M., McMackin, D., Peng, S., Phillips, J., Burke, T., Murphy, S., et al. (1992). Temporal neocorticectomy in management of intractable epilepsy: long-term outcome and predictive factors. *Epilepsia.* 33, 852–61.

(33) Pulsifer, M.B., Brandt, J., Salorio, C.F., Vining, E.P., Carson, B.S., & Freeman, J.M. (2004). The cognitive outcome of hemispherectomy in 71 children. *Epilepsia.* 45, 243–54.

(34) Hermann, B.P., Wyler A.R, & Somes G. (1991). Language Function following anterior temporal lobectomy. *J Neurosurg*.74, 560-66.

(35) Saykin, A. J., Stafiniak, P., Robinson, L. J., Flannery, K. A., Gur, R. C., O'Connor, M. J., & Sperling, M. R.(1995). Language before and after temporal lobectomy: specificity of acute changes and relation to early risk factors. *Epilepsia*. 36, 1071–1077.

(36) Helmstaedter, C., Reuber, M., & Elger, C.C. (2002). Interaction of cognitive aging and memory deficits related to epilepsy surgery. *Ann Neurol*. 52, 89-94.

(37) Hickok G, & Poeppel D. (2004). Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. *Cognition.* 92, 67–99.

(38) Kho, K.H., Indefrey, P., Hagoort, P., Van Veelen, C.W.M., Van Rijen, P.C., & Ramsey, N.F. (2008). Unimpaired sentence comprehension after anterior temporal cortex resection. *Neuropsychologia.* 46, 1170–8.

(39) Simmons, W.K., & Martin, A. (2009). The anterior temporal lobes and the functional architecture of semantic memory. *J Int Neuropsychol Soc*. 15, 645–9.

(40) Jefferies, E., & Lambon, Ralph, M.A. (2006). Semantic impairment in stroke aphasia versus semantic dementia: a case-series comparison. *Brain.*129, 2132–47.

(41) Lambon Ralph,M.A., Ehsan, S., Baker, G.A. & Rogers, T.T. (2012). Semantic memory is impaired in patients with unilateral anterior temporal lobe resection for temporal lobe epilepsy. *Brain*. 135, 242-258.

(42) Baxendale, S. (2002). The role of functional MRI in the presurgical investigation of temporal lobe epilepsy patients: A clinical perspective and review. *Journal of Clinical and Experimental Neuropsychology*. 24, 664-676.

(43) Davies, K.G., Bell, B.D., Bush, A.J., Hermann, B.P., Dohan, F.C. & Jr, Jaap, A.S. (1998). Naming decline after left anterior temporal lobectomy correlates with pathological status of resected hippocampus. *Epilepsia*. 39, 407–19.

(44) Giovagnoli, A.R., Erbetta, A., Villani, F., & Avanzini, G. (2005). Semantic memory in partial epilepsy: verbal and non-verbal deficits and neuroanatomical relationships. *Neuropsychologia*. 43, 1482–92.

(45) Hall, K.E., Isaac, C.L., & Harris, P. (2009). Memory Complaints in epilepsy: An accurate reflection of memory impairment or an indicator of poor adjustment? A review of the literature. *Clinical psychology review.* 29, 354-367.

(46) Andelman. F., Zuckerman-Feldhay.E., Hoffien.D., Fried.I., & Neufeld.M.Y (2004). Lateralisation of deficits in self-awareness of memory in patients with intractable epilepsy. *Epilepsia*. 45, 826-833.

(47) Fargo.J.M., Schefft.B.K.,Szaflarski,J.P.,Dulay,M.F.,Testa,M.S.,Privitera, M.D., & Hwa-Shain,Y. (2004). Accuracy of self-reported neuropsychological functioning in individuals with epileptic or psychogenic nonepileptic seizures. *Epilepsy and Behaviour.* 5,143-150.

(48) Au, A., Leung, P., Kwok, A., Li, P., Lui, C., & Chan, J. (2006). Subjective memory and mood of Hong Kong Chinese adults with epilepsy. *Epilepsy and Behaviour.* 9, 68−72.

(49) Rausch, R. (1985). Differences in cognitive function with left and right temporal lobe dysfunction. In D. F. Benson & E. Zaidel (Eds.), *The dual brain.* New York: Raven Press, pp. 247–261.

(50) Ribbler, A., & Rausch, R. (1990). Performance of patients with unilateral temporal lobectomy on selective reminding procedures using either related or unrelated words. *Cortex*. 26, 575–584.

(51) Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica.* 67, 361–370.

(52) Viskontas, I.V., McAndrews, M.P., & Moscovitch, M. (2002). Memory for famous people in patients with unilateral temporal lobe epilepsy and excisions. *Neuropsychology*. 16, 472–80.

(53) Ives-Deliperi, V.L. & Butler, J.T. (2012). Naming outcomes of anterior temporal lobectomy in epilepsy patients: A systematic review of the literature. *Epilepsy & Behaviour.* 24, 194-198.

(54) Breakwell, G.M.,Johnathan A.S., & Wright, D.B. (2012). *Research Methods in psychology.* (Eds). London.Sage. p.515

(55) Jefferies, E., Patterson, K., Jones, R.W., & Lambon Ralph, M.A. (2009). Comprehension of concrete and abstract words in semantic dementia. *Neuropsychology*. 23, 492–9.

(56) Warrington, E. K. (1996). *The Camden Memory Test Battery*. Hove: Psychology Press.

(57) Pobric, G., Lambon Ralph, M.A., & Jefferies, E. (2009). The role of the anterior temporal lobes in the comprehension of concrete and abstract words: rTMS evidence. *Cortex.* 45, 1104–10.

(58) Pobric, G.G., Jefferies, E., & Lambon Ralph, M.A. (2007). Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. *Proc Natl Acad Sci.*104, 20137–41.

(59) Binney, R.J., Embleton, K.V., Jefferies, E., Parker, G.J.M., & Lambon Ralph, M.A.(2010). The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: evidence from a novel direct comparison of distortion-corrected fMRI, rTMS, and semantic dementia. *Cereb Cortex*. 20, 2728–38.

(60) Bozeat, S., Lambon Ralph, M.A., Patterson, K., Garrard, P., & Hodges, J.R.(2000). Non-verbal semantic impairment in semantic dementia. *Neuropsychologia*. 38, 1207–15.

(61) Lambon Ralph, M.A., Howard, D., Nightingale, G., & Ellis, A.W. (1998). Are living and non-living category-specific deficits causally linked to impaired perceptual or associative knowledge? Evidence from a category-specific double dissociation. *Neurocase*. 4, 311–38.

(62) Warrington, E.K. (1997). The graded naming test: a restandardisation. *Neuropsychological Rehabilitation*. 7, 143–146.

(63) Snaith, R. P., & Zigmond, A. S. (1994). HADS: *Hospital Anxiety and Depression Scale.* Windsor: NFER Nelson

(64) Wechsler, D. (2008). *Wechsler Adult Intelligence Scale–Fourth Edition*. San Antonio, TX: Pearson.

(65) Osterrieth, P. Le test de copie d'une figure complexe.(1944). *Arch Psychologie.* 30, 205–550.

(66) Raven, J.C. (1962). *Coloured progressive matrices: sets A, AB, B.* London: HK Lewis.

(67) Knapp, T.R. (1990). Treating ordinal scales as interval scales: An attempt to resolve the controversy. *Nursing Research*. 39, 121-123.

(68) Clark-Carter, D.C.C. (2010). *Quantitative psychological research, the complete student's companion* (3rd ed.). New York. Psychology press.

(69) Howell, D.C. (2007). *Statistical methods for psychology* (6th ed.).Belmont, C.A: Thomson/Wadsworth.

(70) Cohen, J. (1988). *Statistical power analysis for behavioural sciences* (2nd ed.). Hillsdale, NJ:Lawrence Erlbaum associates, Inc.

(71) Berelson, Bernard. (1952). *Content Analysis in Communication Research*. Glencoe, IL: The Free Press.p.489.

(72) Weber, P.R*. Basic content analysis* (1990). (2nd ed.) Thousand Oaks, Cal, Sage. pp.117-123.

(73) Giovagnoli,A.R., Mascheroni, G., & Avanzini, G. (1997). Self –reporting of everyday memory in patients with epilepsy: relation to neuropsychological, clinical, pathological and treatment factors. *Epilepsy Research*. 28, 119-128.

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

(75) Baker, G.A., Taylor, J., & Hermann, B.P. (2009). How can cognitive status predispose to psychological impairment? *Epilepsy and Behaviour.*15 p.31-35

(76) Lambon Ralph, M.A., McClelland, J.L., Patterson, K., Galton, C.J., & Hodges, J.R. (2001). No right to speak? The relationship between object naming and semantic impairment: neuropsychological abstract evidence and a computational model. *J Cogn Neurosci* .13, 341–56.

(77) Hodges, J.R., Graham, N., & Patterson, K. (1995). Charting the progression in semantic dementia: implications for the organisation of semantic memory. *Memory.* 3, 463–495.

(78) Lambon Ralph, M.A., Sage, K.E., & Roberts, J. (2000). Classical anomia: a neuropsychological perspective on speech production. *Neuropsychologia.* 38 186-202.

(79) Thompson, P.J. (1989). Epilepsy and memory. In: Manelis J, Bental E, Loeber JN, Dreyfuss FE, eds. *Advances in Epileptology*, Vol. 17. Raven Press, New York, pp.404-406.

(80) Vermeulen, J., Aldenkamp, A.P., & Alpherts, W.C.J. (1993). Memory complaints in epilepsy: correlations with cognitive performance and neuroticism. *Epilepy Research.* 15,157-170.

(81) Piazzini, A., Canevini, M.P., Maggiori, G., & Canger, R. (2001). Depression and Anxiety in Patients with Epilepsy. *Epilepsy Behaviour.* 5, 481-489.

(82) Beyenburg, S., Mitchell, A.J., Schmidt, D., Elger, C.E, & Reuber, M. (2005). Anxiety in patients with epilepsy: systematic review and suggestions for clinical management. *Epilepsy and Behavior*. 2, 161-71.

(83) Paradiso, S., Hermann, B.P., Blumer, D., Davies, K., & Robinson, R.G. (2001). Impact of depressed mood on neuropsychological status in temporal lobe epilepsy. *Journal Neurol Neurosurg Psychiatry.* 70, 180-185.

(84) Altshuler, L., Rausch, R., Delrahim, S., Kay, J., Crandall, P. (1999). Temporal lobe epilepsy,temporal lobectomy, and major depression. *Journal of Neurology, Neurosurgery, and Psychiatry.* 11, 436–43.

(85) Hermann, B.P., Wyler, A.R., & Somes. G. (1992). Preoperative psychological adjustment and surgical outcome are determinants of psychological status after anterior temporal lobectomy. *Journal of Neurology, Neurosurgery, and Psychiatry*. 55, 491-496.

(86) Crail-Meléndez, D., Herrera-Melo, A., Martínez-Juárez, I.E., & Ramírez-Bermúdez, J. (2012). Cognitive-behavioral therapy for depression in patients with temporal lobe epilepsy: a pilot study. *Epilepsy Behav.* 23, 52–56.

(87) National Institute for Clinical Excellence. (2004). Depression: *Management of*
depression in primary and secondary care—National clinical practice guideline number 23. London: National Collaborating Centre for Mental Health.

(88) Hamberger, M.J., Goodman, R.R., Perrine, K., & Tamny, T. (2001). Anatomic dissociation of auditory and visual naming in the lateral temporal cortex. *Neurology.* 56, 56–61.

(89) Patterson, K., & Hodges, J. R. (1995). Disorders of semantic memory. In A. D. Baddeley, B. A. Wilson, & F. N. Watts (Eds.), *Handbook of memory disorders*. Chichester: John Wiley and Sons, pp. 167–186.

(90) Meldolesi, G.N., Di Gennaro, G., Quarato, P.P., Esposito, V., Grammaldo, L.G., Morosini, P., et al. (2007). Changes in depression, anxiety, anger, and personality after resective surgery for drug-resistant temporal lobe epilepsy: a 2-year follow-up study. *Epilepsy Res*. 77:22–30.

Appendix 2A:Self-report TLE surgery questionnaire

Please answer the following questions using a scale of 1-10 to signify whether you have experienced these problems since your surgery?

Frequency: 0 – Never, 3 – Rarely, 5 –Sometimes, 8– Often, 10 – Always

1) Have you experienced any problems remembering things?

---

2) Have you experienced any problems with understanding conversations?

---

3) Do you have any problems recognising or naming objects e.g. everyday objects

---

---

4) Have you had any problem with understanding written information?

---

5) Have you experienced any problems with your mood or behaviour?

---

6) Have you experienced any other problems since the surgery?

Many Thanks

Appendix 2B: Background checks of the data

Statistics

		GNT	namingaccuracy	namingRTs	problems_remembering	Synonymaccuracy	SynonymRTs	problems_understanding_conversations	problems_understanding_written_information	Camden_words	Camden_faces	problems_with_recognising_objects	mood_and_behaviour
N	Valid	20	20	20	20	20	20	20	20	20	20	20	16
	Missing	0	0	0	0	0	0	0	0	0	0	0	4
Mean		15.8500	.9386	2.4588	3.7500	.8594	4.6134	1.6500	2.0500	20.2500	23.3000	.9500	2.1250
Median		15.5000	.9500	2.0617	5.0000	.8750	4.2135	.0000	.0000	21.0000	24.0000	.0000	.0000
Mode		13.00	.98	1.28[a]	5.00	.92	7.58	.00	.00	22.00	23.00[a]	.00	.00
Std. Deviation		4.36825	.04602	1.01147	3.25859	.06461	2.52127	2.32322	3.11997	2.29129	2.25015	1.84890	3.03040
Skewness		.407	-2.264	1.188	.288	-.779	1.821	.893	1.254	-.720	-2.849	1.746	1.359
Std. Error of Skewness		.512	.512	.512	.512	.512	.512	.512	.512	.512	.512	.512	.564
Minimum		7.00	.78	1.28	.00	.72	1.91	.00	.00	15.00	15.00	.00	.00
Maximum		26.00	.98	4.75	10.00	.94	12.57	6.00	10.00	24.00	25.00	5.00	10.00

a. Multiple modes exist. The smallest value is shown

Statistics

		HADS_anxiety	HADS_depression
N	Valid	13	13
	Missing	7	7
Mean		9.231	7.000
Median		9.000	6.000
Mode		5.0[a]	4.0
Std. Deviation		4.5489	4.6188
Skewness		.269	1.559
Std. Error of Skewness		.616	.616
Kurtosis		.197	2.876
Std. Error of Kurtosis		1.191	1.191
Range		17.0	17.0
Minimum		1.0	2.0
Maximum		18.0	19.0
Sum		120.0	91.0

a. Multiple modes exist. The smallest value is shown

Appendix 2B: Background checks of the data

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Std. Error	Statistic	Std. Error
GNT	20	7.00	26.00	15.8500	.97677	4.36825	.407	.512	.659	.992
namingaccuracy	20	.78	.98	.9386	.01029	.04602	-2.264	.512	7.021	.992
namingRTs	20	1.28	4.75	2.4588	.22617	1.01147	1.188	.512	.369	.992
Synonymaccuracy	20	.72	.94	.8594	.01445	.06461	-.779	.512	-.390	.992
SynonymRTs	20	1.91	12.57	4.6134	.56377	2.52127	1.821	.512	4.272	.992
Camden_words	20	15.00	24.00	20.2500	.51235	2.29129	-.720	.512	.255	.992
Camden_faces	20	15.00	25.00	23.3000	.50315	2.25015	-2.849	.512	10.066	.992
Valid N (listwise)	20									

Descriptive Statistics

	N	Minimum	Maximum	Mean		Std. Deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Std. Error	Statistic	Std. Error
problems_remembering	20	.00	10.00	3.7500	.72864	3.25859	.288	.512	-.611	.992
problems_understanding_conversations	20	.00	6.00	1.6500	.51949	2.32322	.893	.512	-1.105	.992
problems_understanding_written_information	20	.00	10.00	2.0500	.69765	3.11997	1.254	.512	.498	.992
problems_with_recognising_objects	20	.00	5.00	.9500	.41343	1.84890	1.746	.512	1.541	.992
mood_and_behaviour	16	.00	10.00	2.1250	.75760	3.03040	1.359	.564	1.377	1.091
Valid N (listwise)	16									

Appendix 2B: Background checks of the data

GNT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	7.00	1	5.0	5.0	5.0
	10.00	1	5.0	5.0	10.0
	13.00	4	20.0	20.0	30.0
	14.00	3	15.0	15.0	45.0
	15.00	1	5.0	5.0	50.0
	16.00	3	15.0	15.0	65.0
	17.00	2	10.0	10.0	75.0
	19.00	1	5.0	5.0	80.0
	21.00	2	10.0	10.0	90.0
	22.00	1	5.0	5.0	95.0
	26.00	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

namingRTs

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1.28	1	5.0	5.0	5.0
	1.46	1	5.0	5.0	10.0
	1.56	1	5.0	5.0	15.0
	1.75	1	5.0	5.0	20.0
	1.83	1	5.0	5.0	25.0
	1.86	1	5.0	5.0	30.0
	1.87	1	5.0	5.0	35.0
	1.91	1	5.0	5.0	40.0
	2.01	1	5.0	5.0	45.0
	2.05	1	5.0	5.0	50.0
	2.07	1	5.0	5.0	55.0
	2.10	1	5.0	5.0	60.0
	2.24	1	5.0	5.0	65.0
	2.35	1	5.0	5.0	70.0
	3.07	1	5.0	5.0	75.0
	3.18	1	5.0	5.0	80.0
	3.22	1	5.0	5.0	85.0
	4.22	1	5.0	5.0	90.0
	4.41	1	5.0	5.0	95.0
	4.75	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

namingaccuracy

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.78	1	5.0	5.0	5.0
	.89	1	5.0	5.0	10.0
	.91	1	5.0	5.0	15.0
	.91	1	5.0	5.0	20.0
	.92	1	5.0	5.0	25.0
	.92	1	5.0	5.0	30.0
	.94	3	15.0	15.0	45.0
	.95	4	20.0	20.0	65.0
	.95	1	5.0	5.0	70.0
	.97	1	5.0	5.0	75.0
	.98	5	25.0	25.0	100.0
	Total	20	100.0	100.0	

Appendix 2B: Background checks of the data

problems_remembering

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.00	7	35.0	35.0	35.0
	3.00	1	5.0	5.0	40.0
	5.00	9	45.0	45.0	85.0
	7.00	1	5.0	5.0	90.0
	10.00	2	10.0	10.0	100.0
	Total	20	100.0	100.0	

Synonymaccuracy

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.72	1	5.0	5.0	5.0
	.75	1	5.0	5.0	10.0
	.77	1	5.0	5.0	15.0
	.78	1	5.0	5.0	20.0
	.81	1	5.0	5.0	25.0
	.82	1	5.0	5.0	30.0
	.84	2	10.0	10.0	40.0
	.86	1	5.0	5.0	45.0
	.88	2	10.0	10.0	55.0
	.90	2	10.0	10.0	65.0
	.91	2	10.0	10.0	75.0
	.92	3	15.0	15.0	90.0
	.94	2	10.0	10.0	100.0
	Total	20	100.0	100.0	

Appendix 2B: Background checks of the data

SynonymRTs

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1.91	1	5.0	5.0	5.0
	2.03	1	5.0	5.0	10.0
	2.29	1	5.0	5.0	15.0
	2.62	1	5.0	5.0	20.0
	2.85	1	5.0	5.0	25.0
	3.00	1	5.0	5.0	30.0
	3.15	1	5.0	5.0	35.0
	3.45	1	5.0	5.0	40.0
	3.98	1	5.0	5.0	45.0
	4.02	1	5.0	5.0	50.0
	4.40	1	5.0	5.0	55.0
	4.47	1	5.0	5.0	60.0
	4.60	1	5.0	5.0	65.0
	4.65	1	5.0	5.0	70.0
	4.71	1	5.0	5.0	75.0
	5.34	1	5.0	5.0	80.0
	7.05	1	5.0	5.0	85.0
	7.58	2	10.0	10.0	95.0
	12.57	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

problems_understanding_conversations

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.00	12	60.0	60.0	60.0
	1.00	1	5.0	5.0	65.0
	2.00	1	5.0	5.0	70.0
	4.00	1	5.0	5.0	75.0
	5.00	4	20.0	20.0	95.0
	6.00	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

Camden_words

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	15.00	1	5.0	5.0	5.0
	16.00	1	5.0	5.0	10.0
	18.00	2	10.0	10.0	20.0
	19.00	3	15.0	15.0	35.0
	20.00	2	10.0	10.0	45.0
	21.00	4	20.0	20.0	65.0
	22.00	5	25.0	25.0	90.0
	23.00	1	5.0	5.0	95.0
	24.00	1	5.0	5.0	100.0
	Total	20	100.0	100.0	

Appendix 2B: Background checks of the data

Camden_faces

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	15.00	1	5.0	5.0	5.0
	21.00	1	5.0	5.0	10.0
	22.00	1	5.0	5.0	15.0
	23.00	6	30.0	30.0	45.0
	24.00	5	25.0	25.0	70.0
	25.00	6	30.0	30.0	100.0
	Total	20	100.0	100.0	

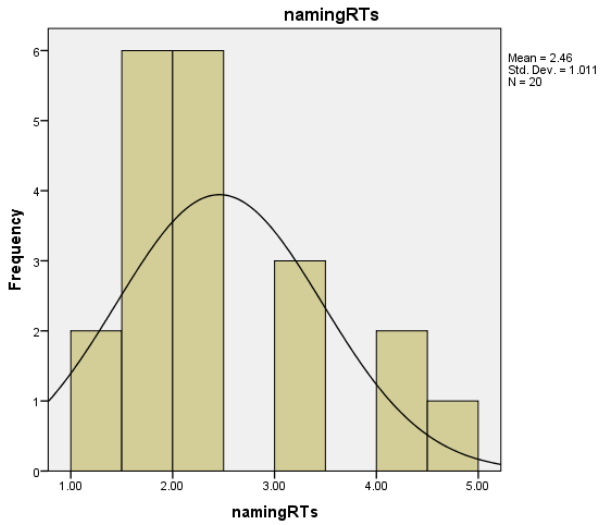
problems_with_recognising_objects

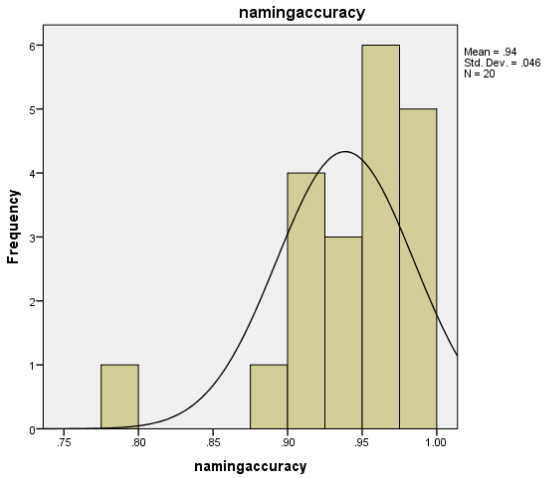
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.00	15	75.0	75.0	75.0
	2.00	2	10.0	10.0	85.0
	5.00	3	15.0	15.0	100.0
	Total	20	100.0	100.0	

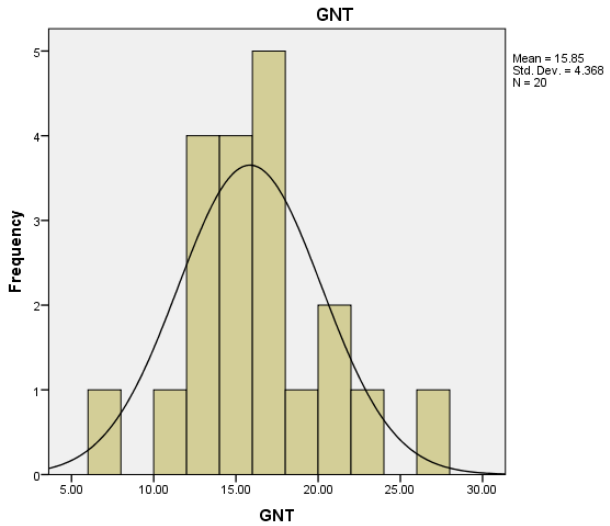
mood_and_behaviour

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	.00	9	45.0	56.3	56.3
	1.00	1	5.0	6.3	62.5
	3.00	1	5.0	6.3	68.8
	5.00	4	20.0	25.0	93.8
	10.00	1	5.0	6.3	100.0
	Total	16	80.0	100.0	
Missing	System	4	20.0		
Total		20	100.0		

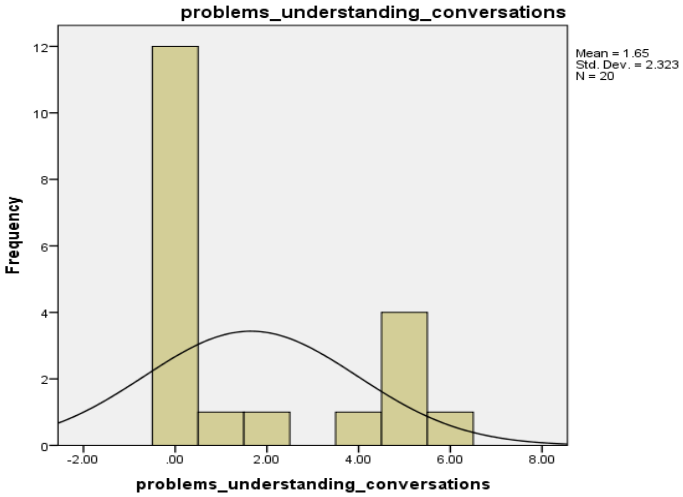
Appendix 2B: Background checks of the data Histograms

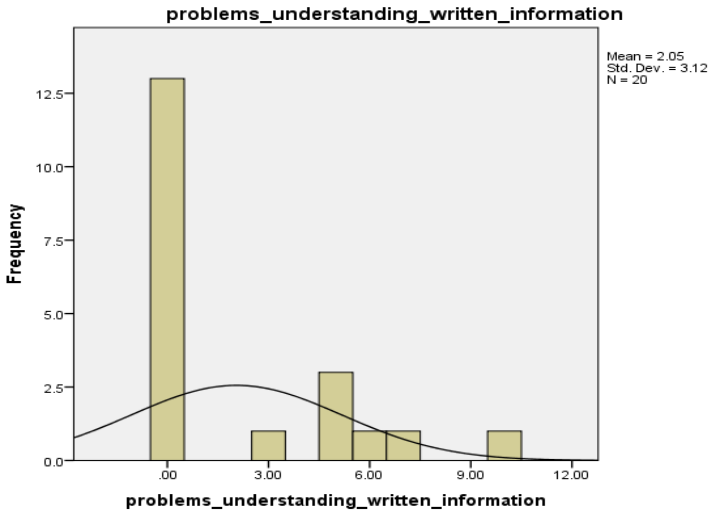


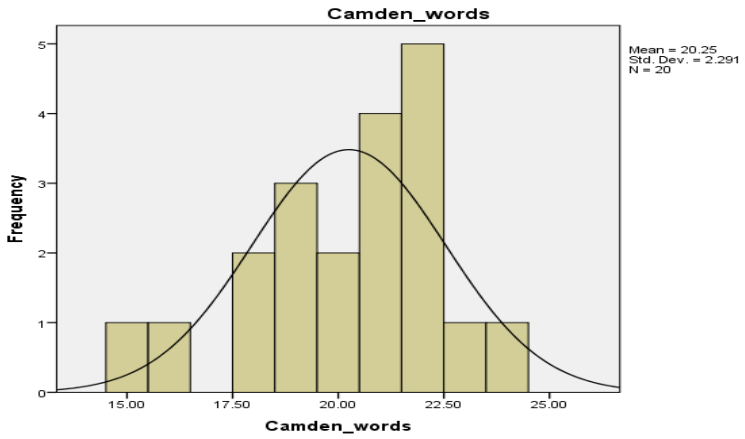




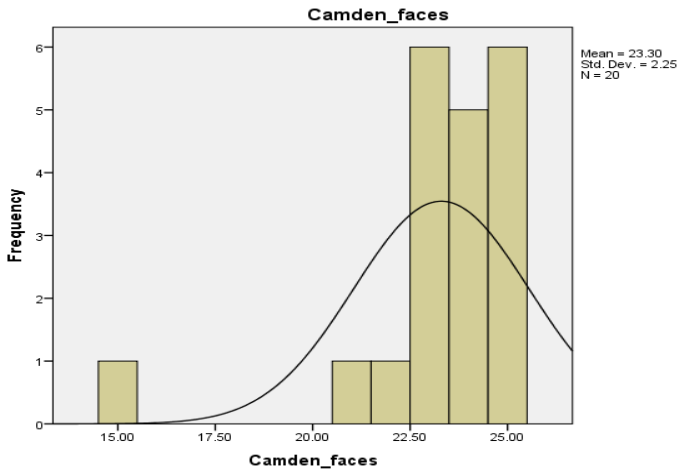
Appendix 2B: Background checks of the data

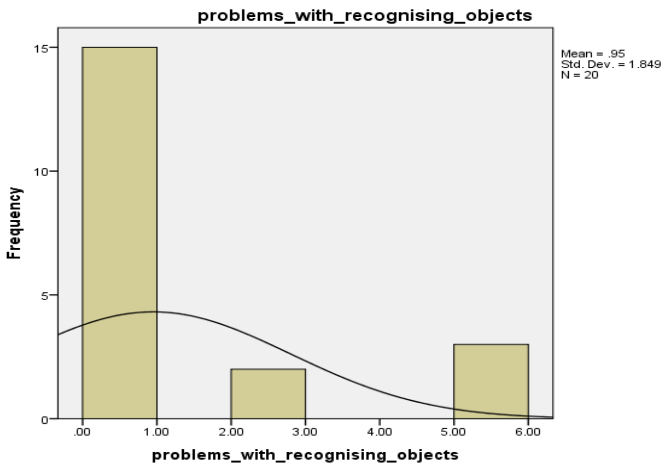




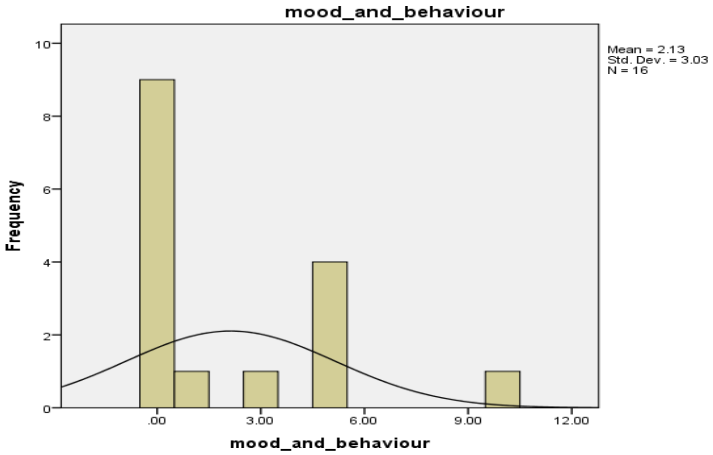


Appendix 2B: Background checks of the data





Appendix 2B: Background checks of the data



Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
GNT	.182	16	.165	.943	16	.388
namingaccuracy	.218	16	.041	.774	16	.001
namingRTs	.224	16	.031	.889	16	.053
problems_remembering	.292	16	.001	.839	16	.009
Synonymaccuracy	.150	16	.200*	.907	16	.106
SynonymRTs	.214	16	.049	.861	16	.020
problems_understanding_conversations	.302	16	.000	.751	16	.001
problems_understanding_written_information	.343	16	.000	.771	16	.001
Camden_words	.153	16	.200*	.940	16	.355
Camden_faces	.292	16	.001	.695	16	.000
problems_with_recognising_objects	.410	16	.000	.618	16	.000
mood_and_behaviour	.321	16	.000	.728	16	.000

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

Appendix 2B: Background checks of the data

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HADS_anxiety	.136	13	.200*	.975	13	.947

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

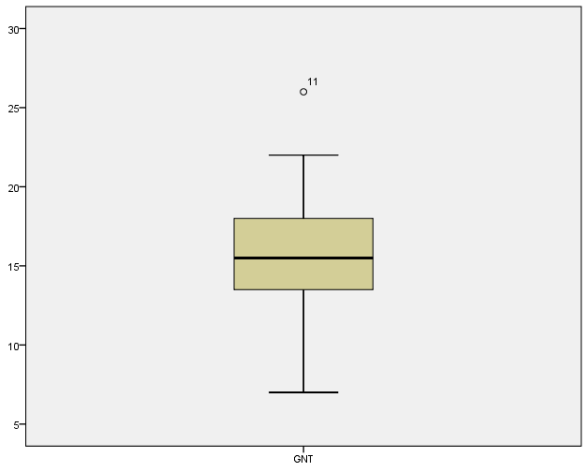
Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
HADS_depression	.204	13	.144	.849	13	.028

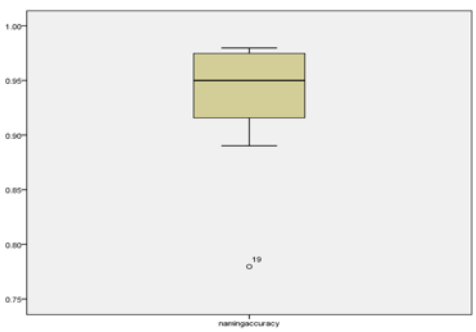
a. Lilliefors Significance Correction

Outliers

Measure: Graded naming test

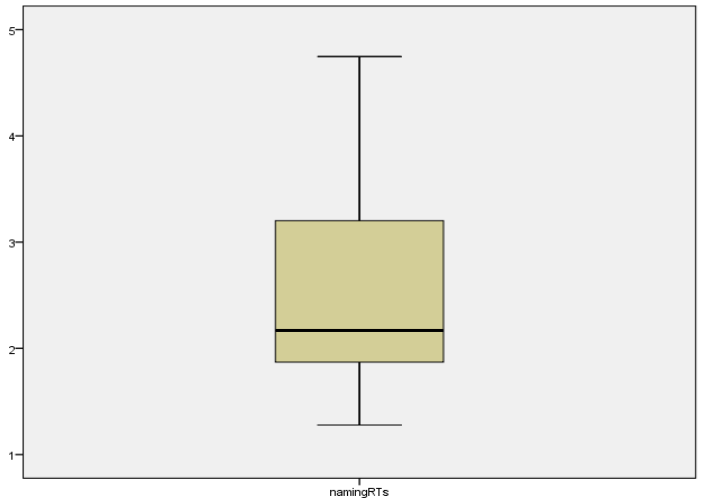


Naming Accuracy

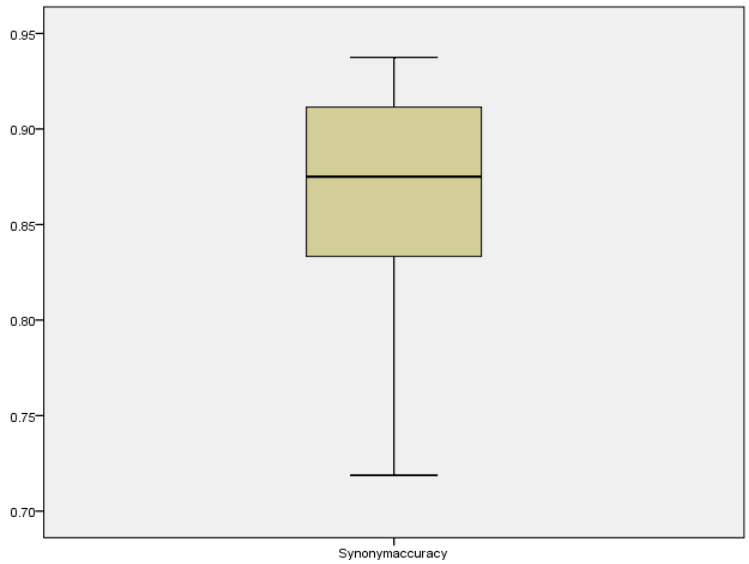


Appendix 2B: Background checks of the data

Naming Speed

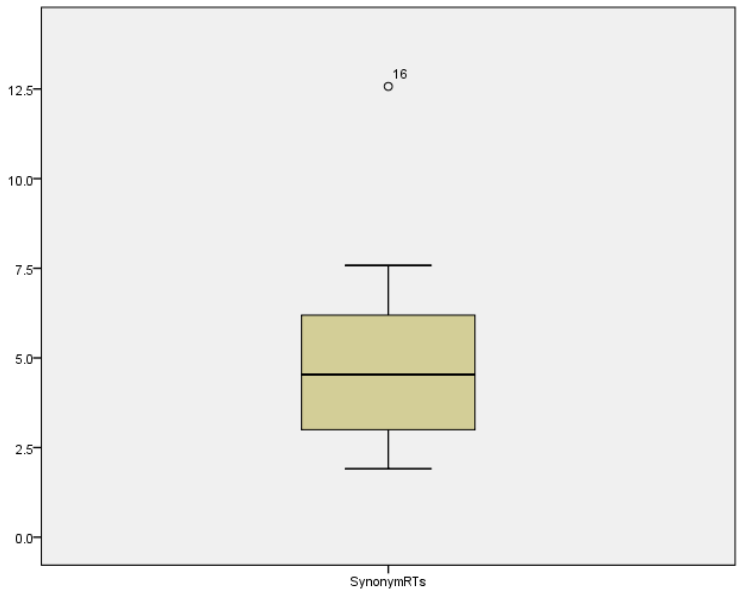


Synonym Judgement task -accuracy

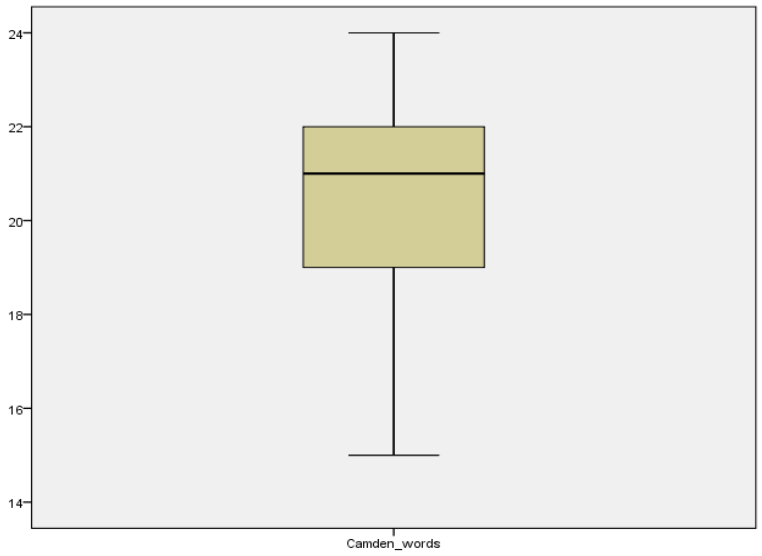


Appendix 2B: Background checks of the data

Synonym Judgement task speed

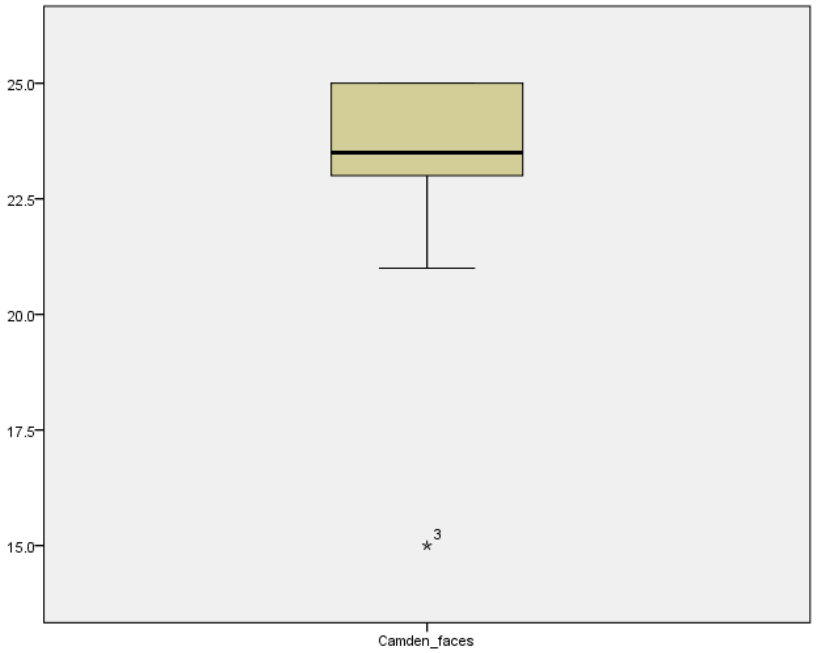


Camden Words



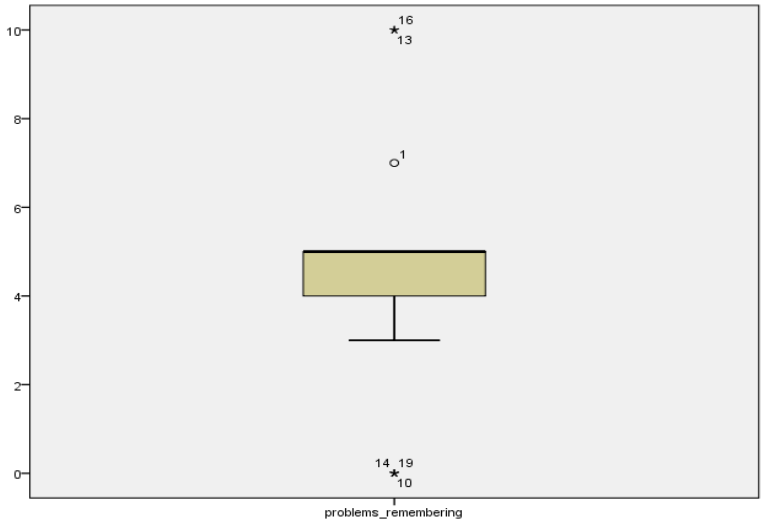
Appendix 2B: Background checks of the data

Camden Faces



Questions from the Self-Report Measure

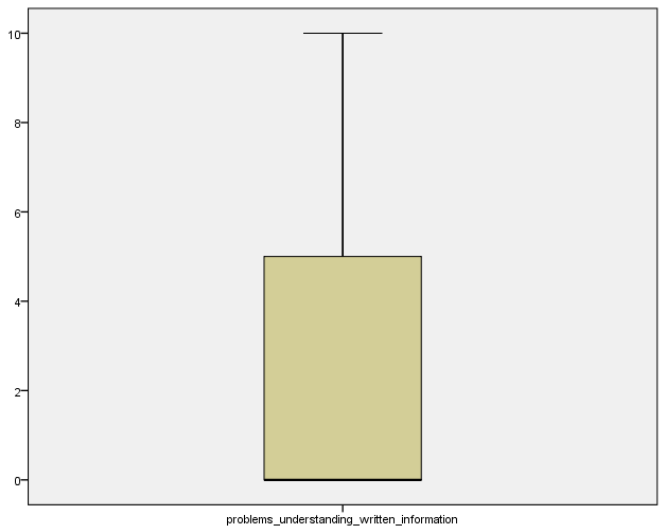
1. Problems Remembering



Appendix 2B: Background checks of the data

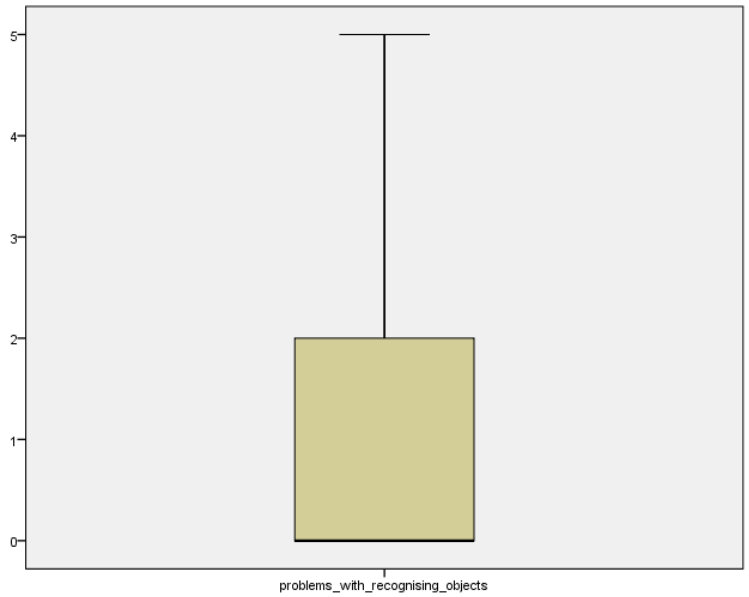
Problems Understanding Conversations

Problems Understanding Written Information

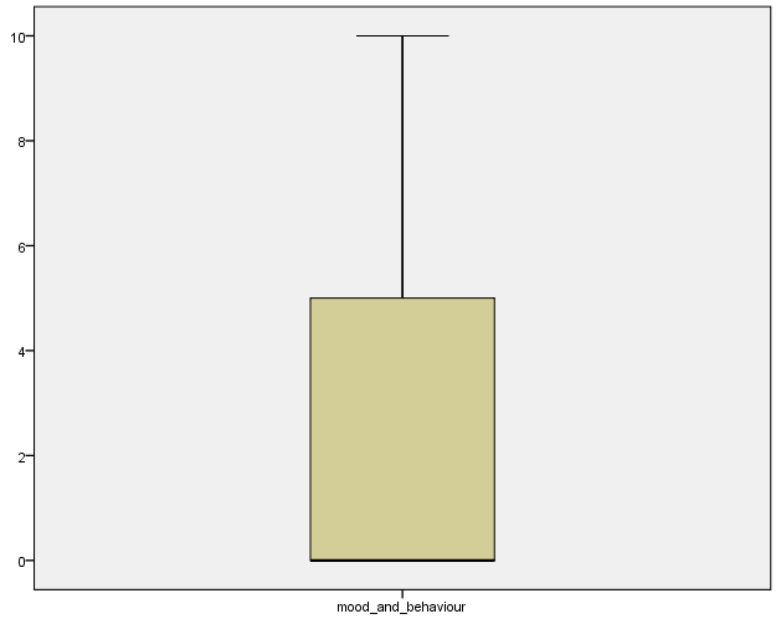


Appendix 2B: Background checks of the data

Problems Recognising Objects



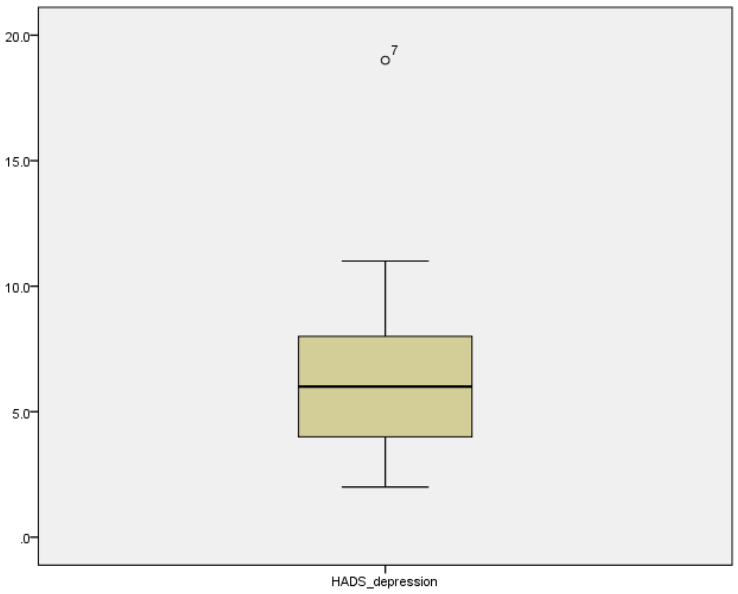
Mood or Behaviour

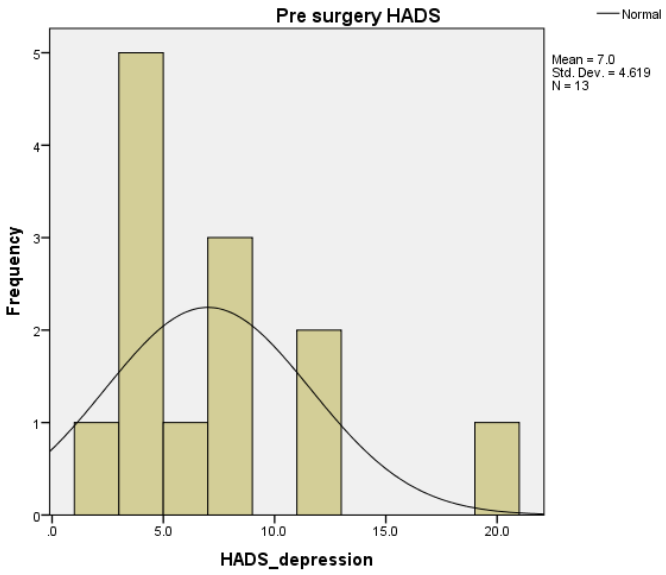


Appendix 2B: Background checks of the data

Pre surgery Hospital Anxiety and Depression Scale

Depression

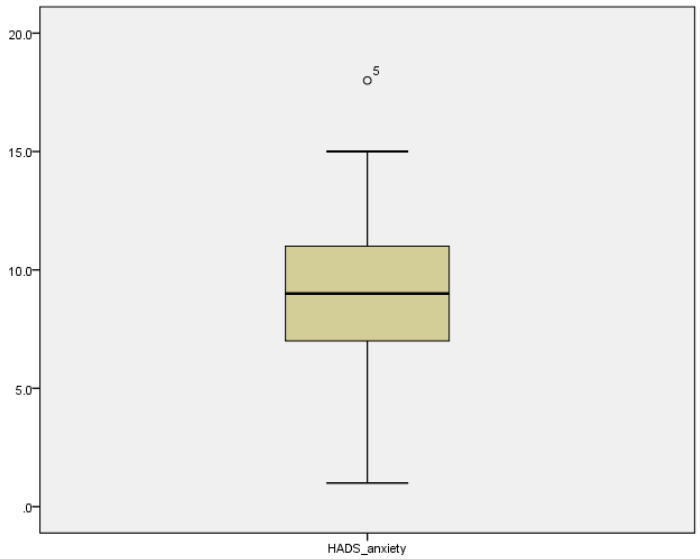


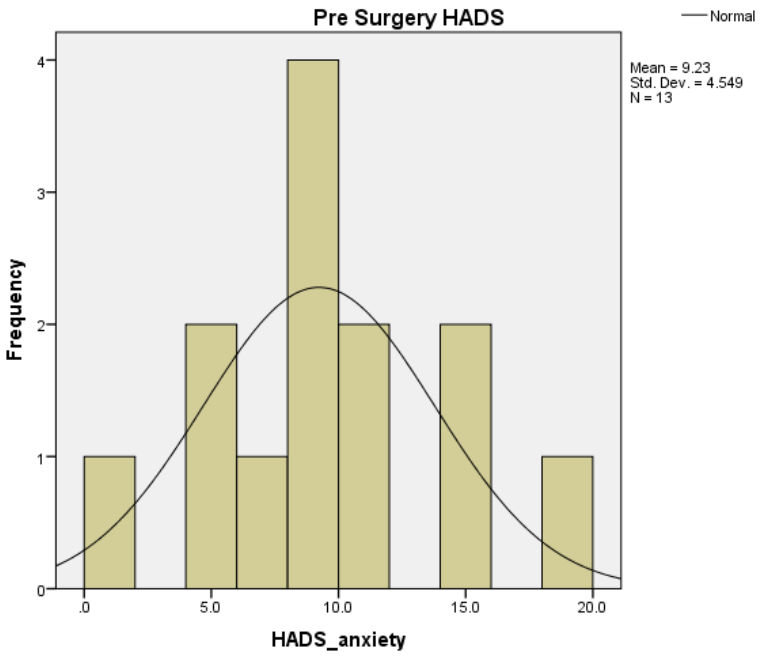


Appendix 2B: Background checks of the data

Pre surgery Hospital Anxiety and Depression Scale

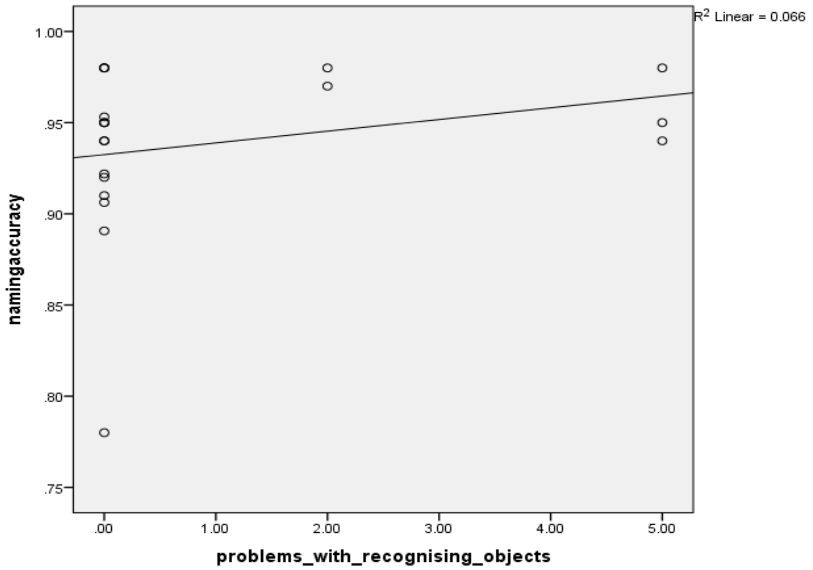
Anxiety

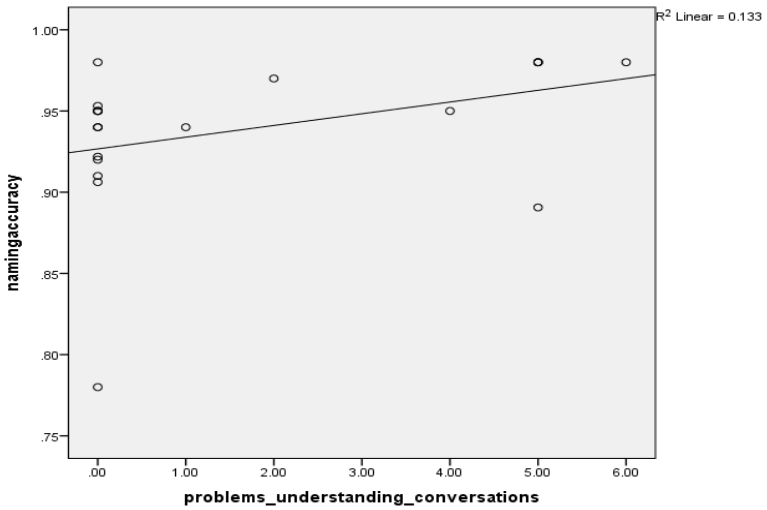




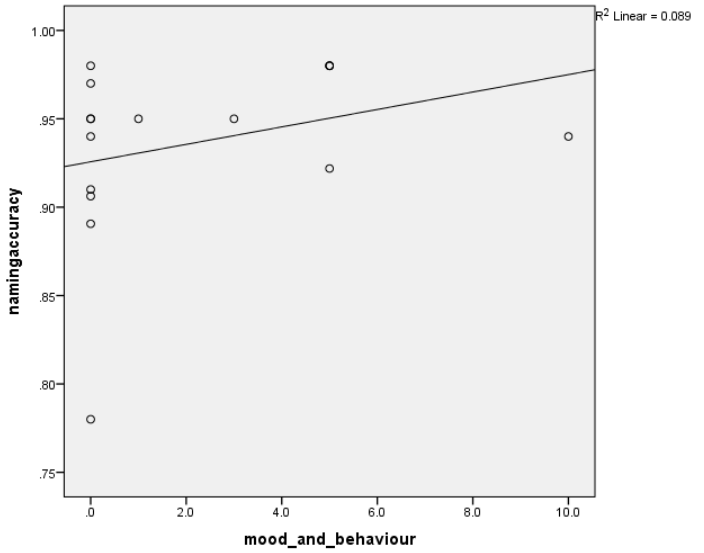
Appendix 2C: Checks for running correlational design

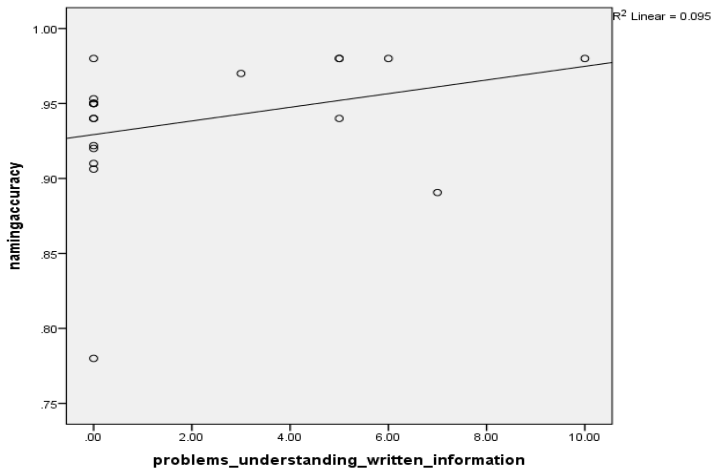
Naming Accuracy & Self Report Measures

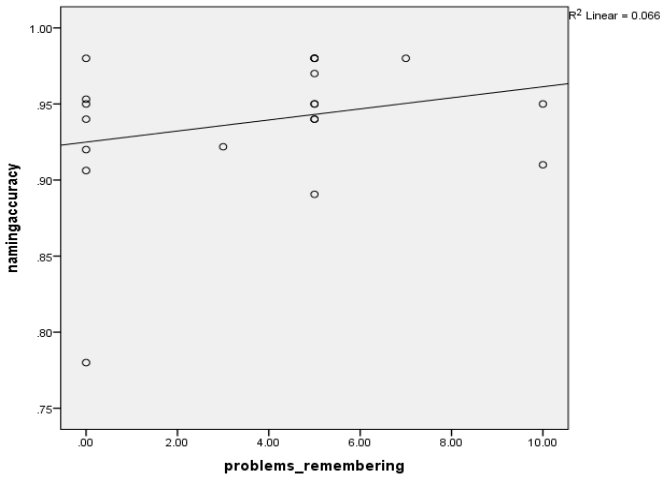




Appendix 2C: Checks for running correlational design

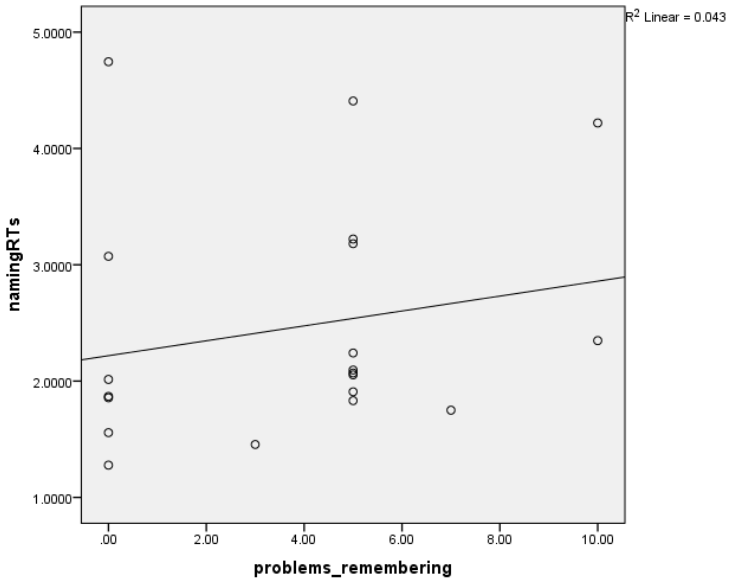


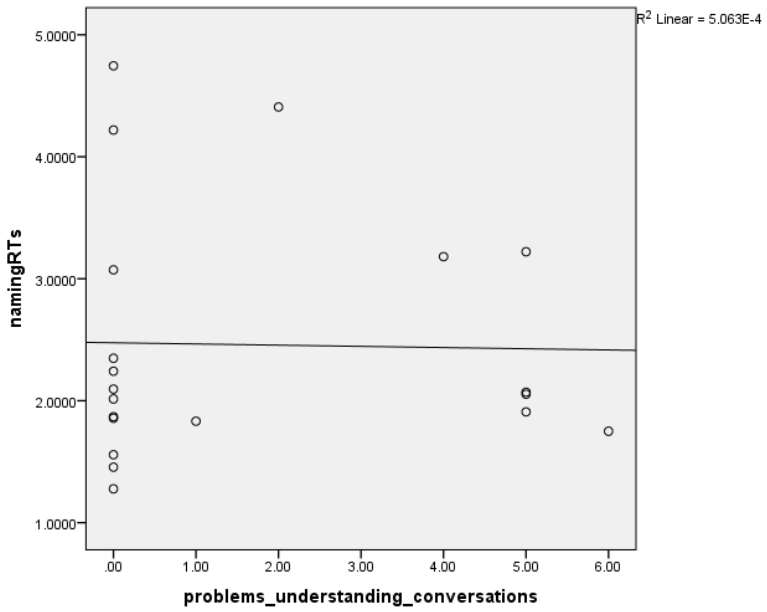




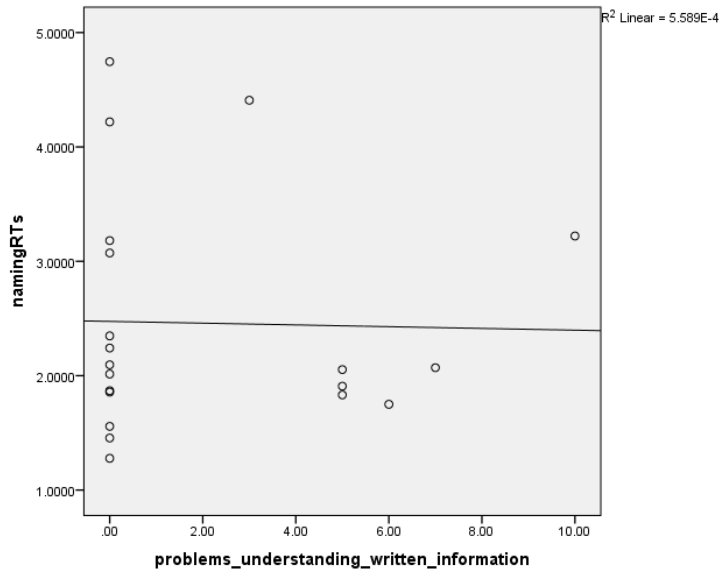
Appendix 2C: Checks for running correlational design

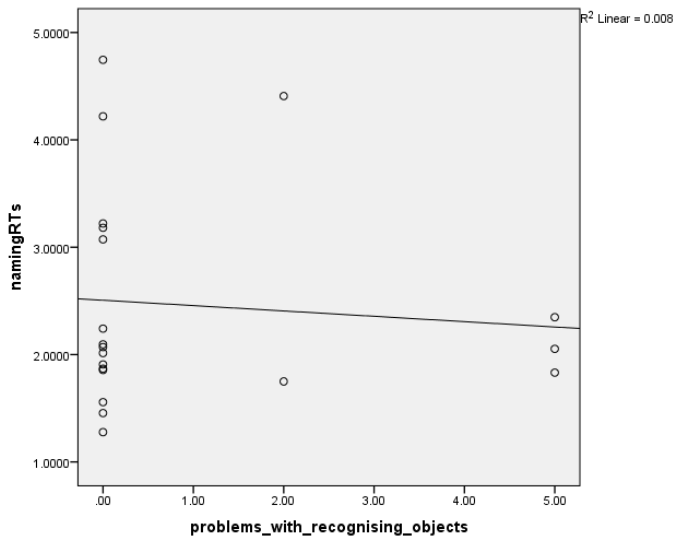
Naming Speed & Self Report Measures



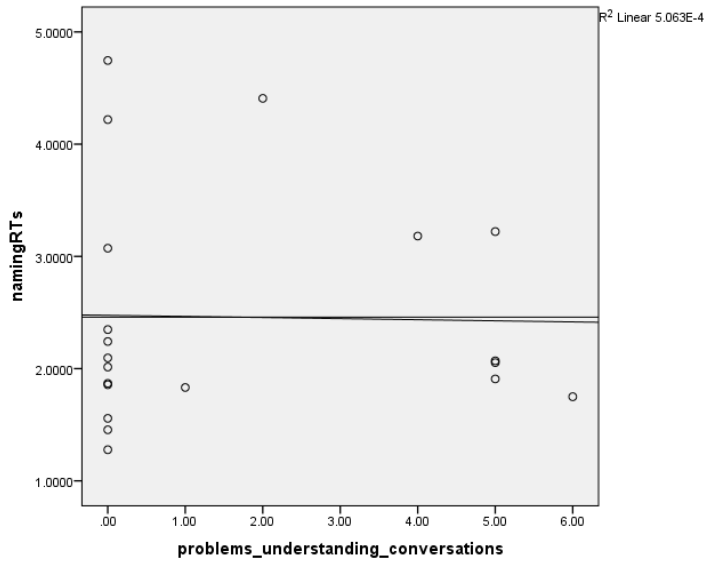


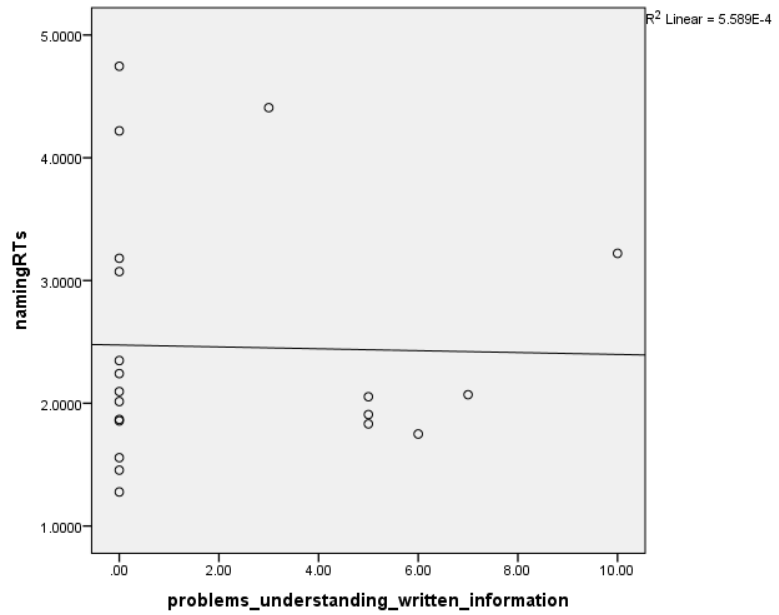
Appendix 2C: Checks for running correlational design



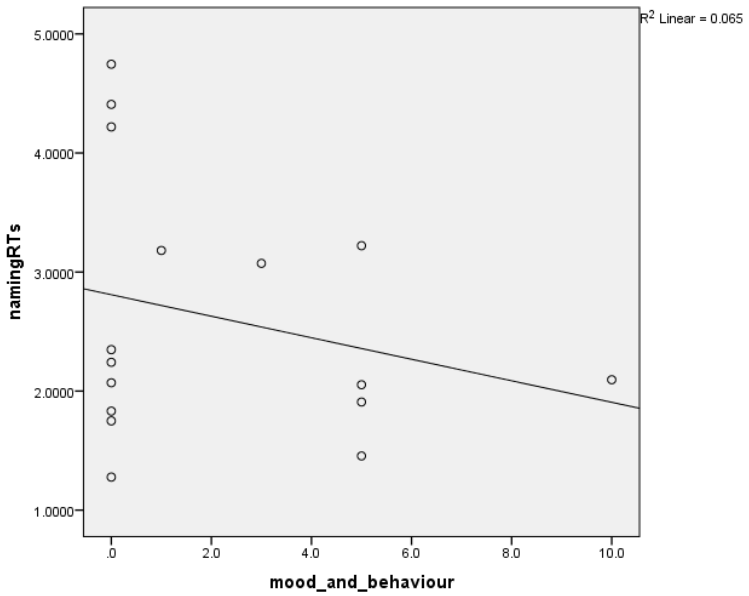


Appendix 2C: Checks for running correlational design

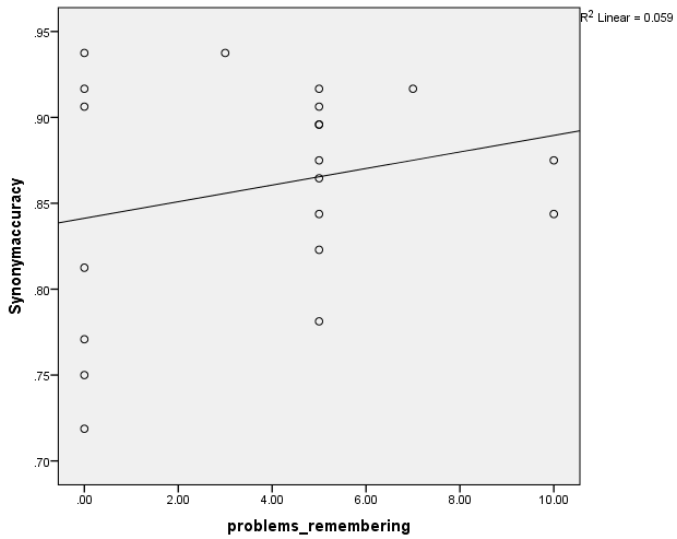




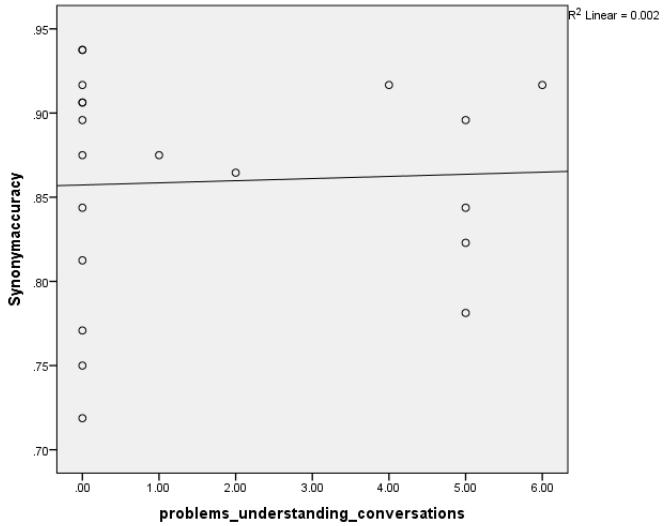
Appendix 2C: Checks for running correlational design

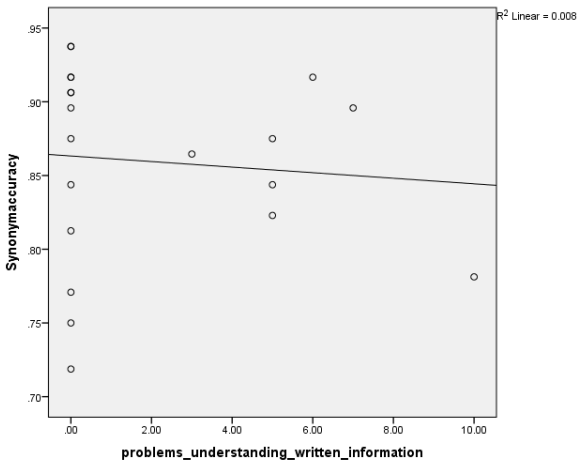


Synonym Accuracy & Self Report Measures

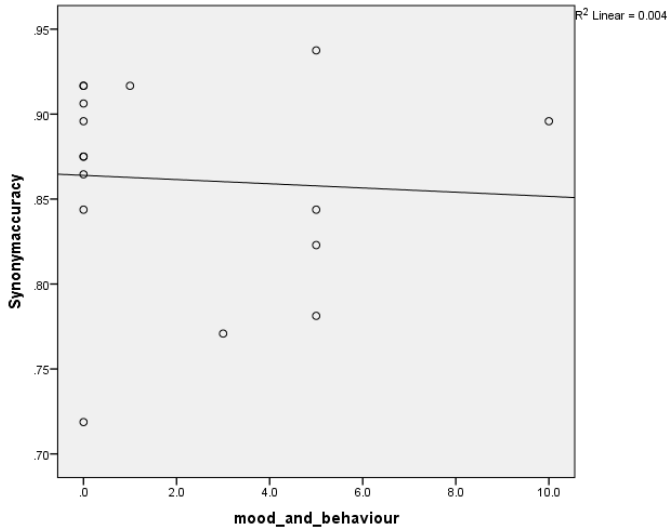


Appendix 2C: Checks for running correlational design

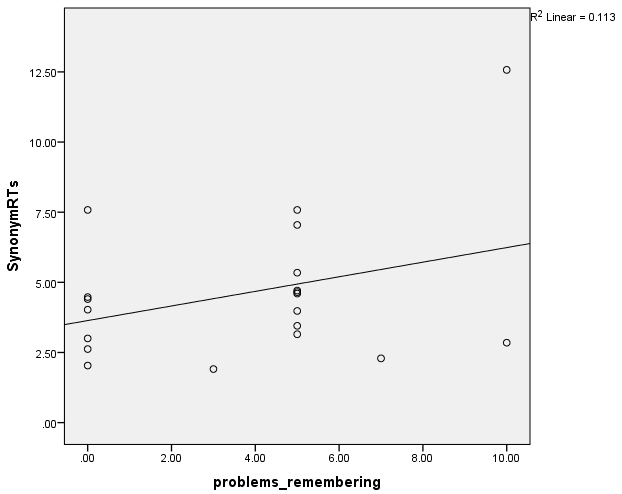




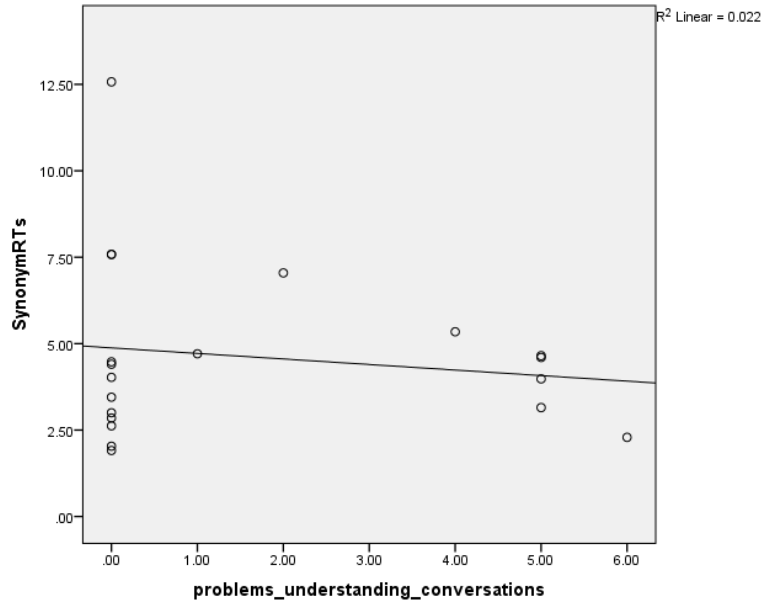
Appendix 2C: Checks for running correlational design

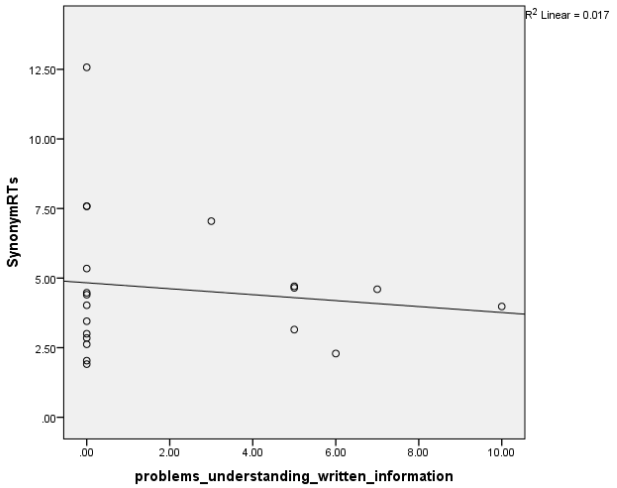


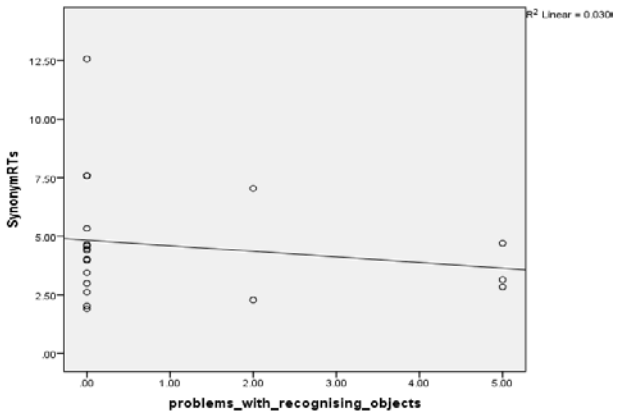
Synonym Naming Speed & Self report measure



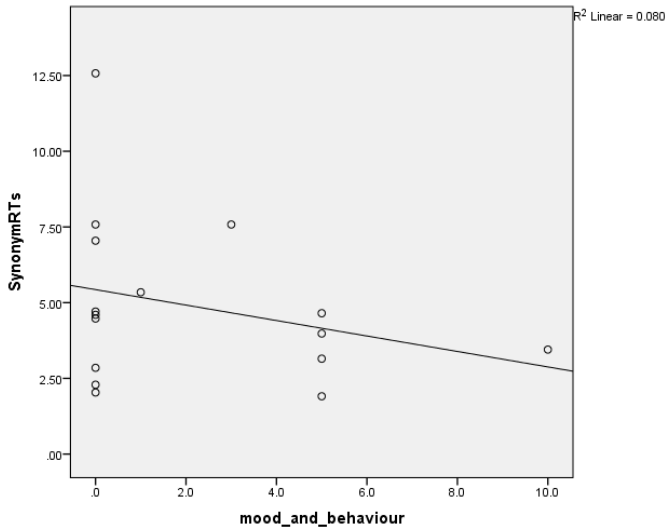
Appendix 2C: Checks for running correlational design



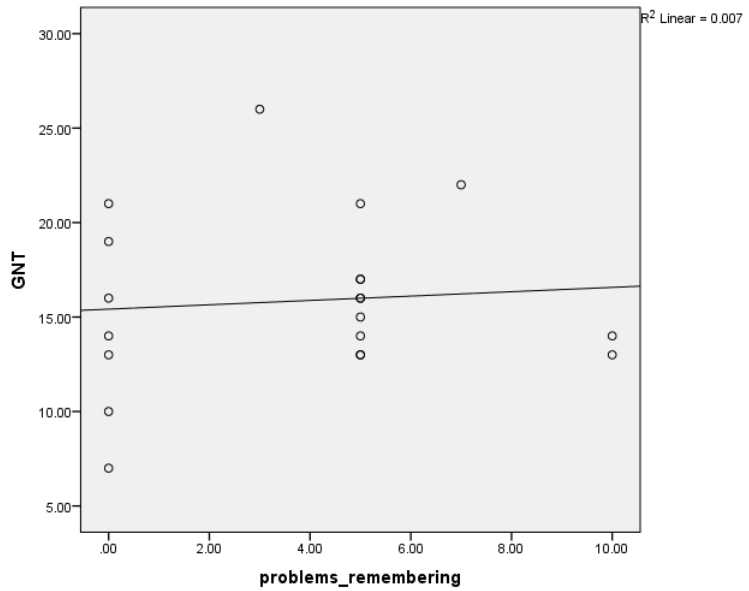




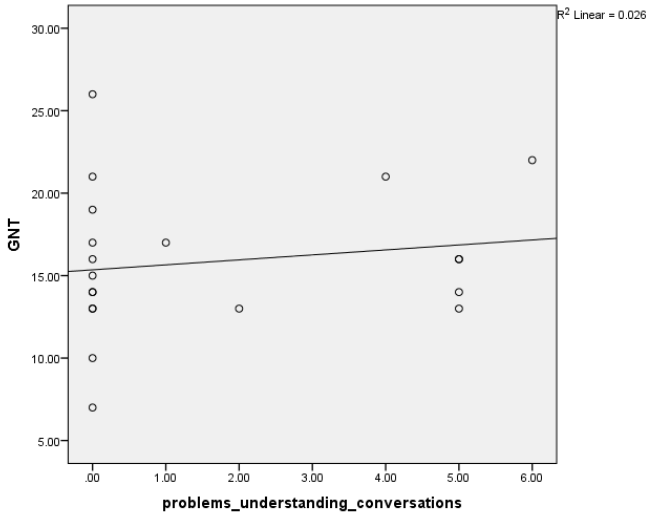
Appendix 2C: Checks for running correlational design

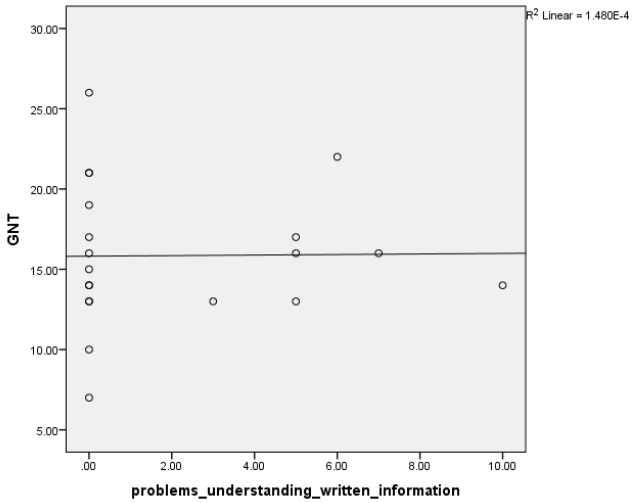


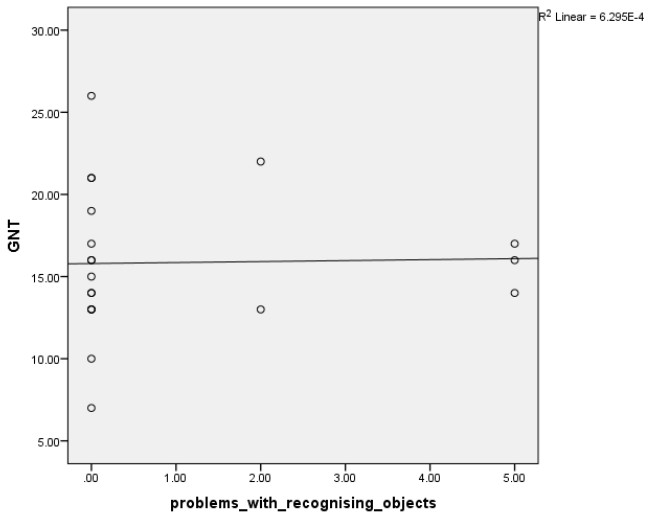
Graded Naming Tests & Self report measure



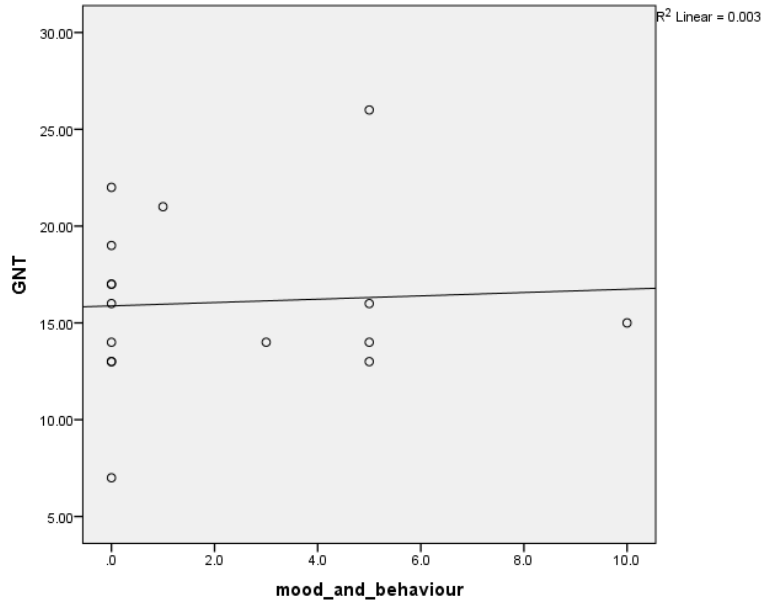
Appendix 2C: Checks for running correlational design



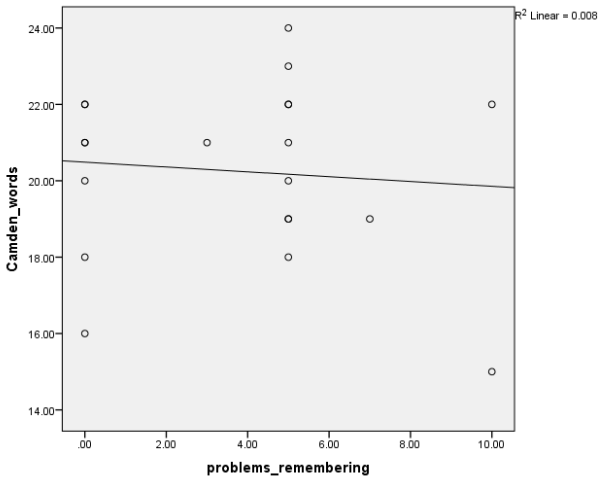




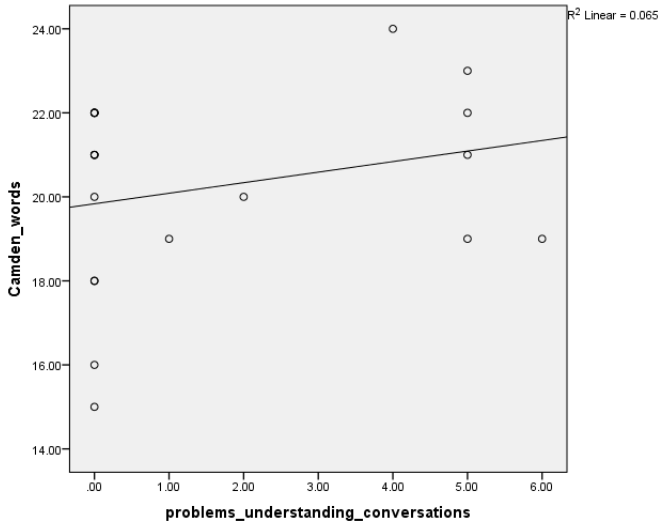
Appendix 2C: Checks for running correlational design

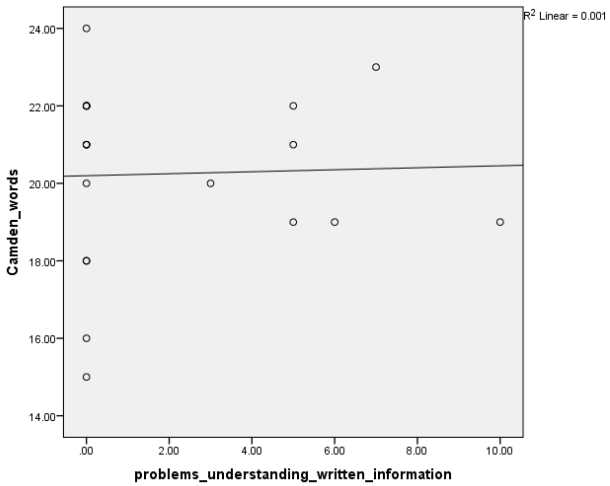


Camden Words Test & Self Report Measure

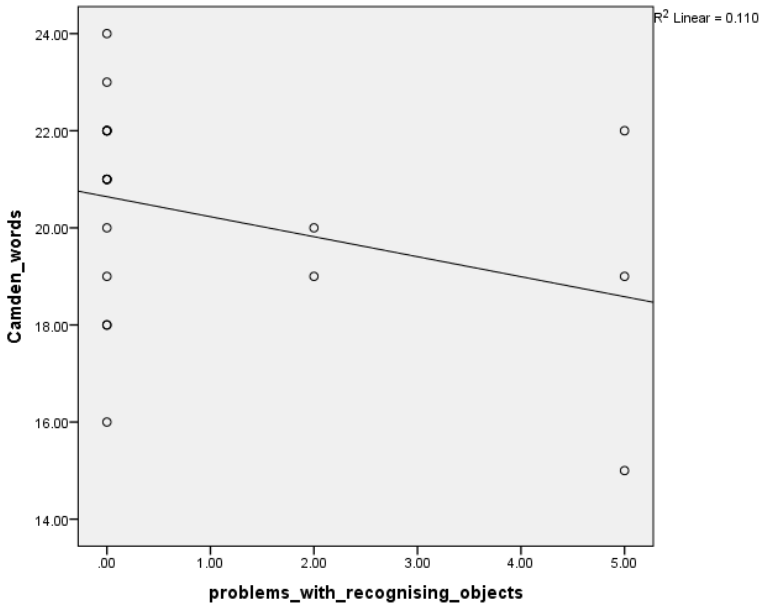


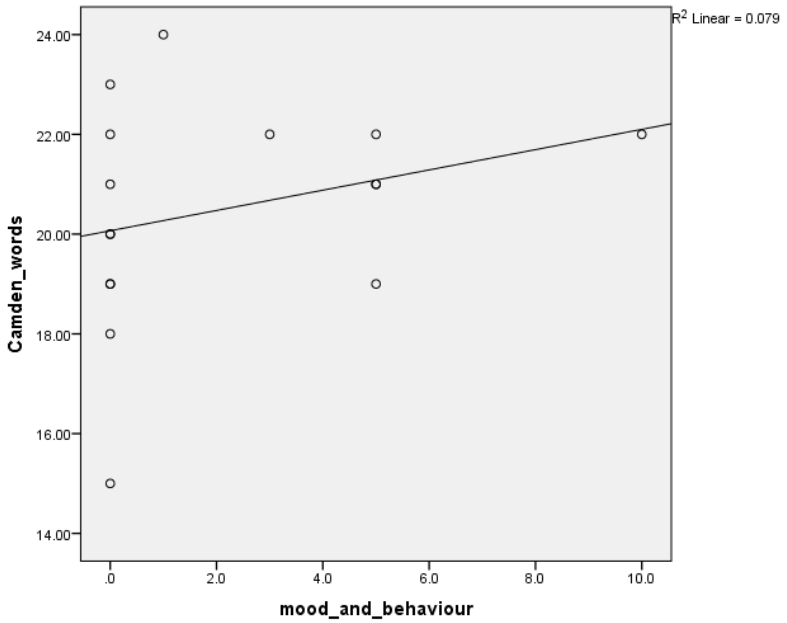
Appendix 2C: Checks for running correlational design





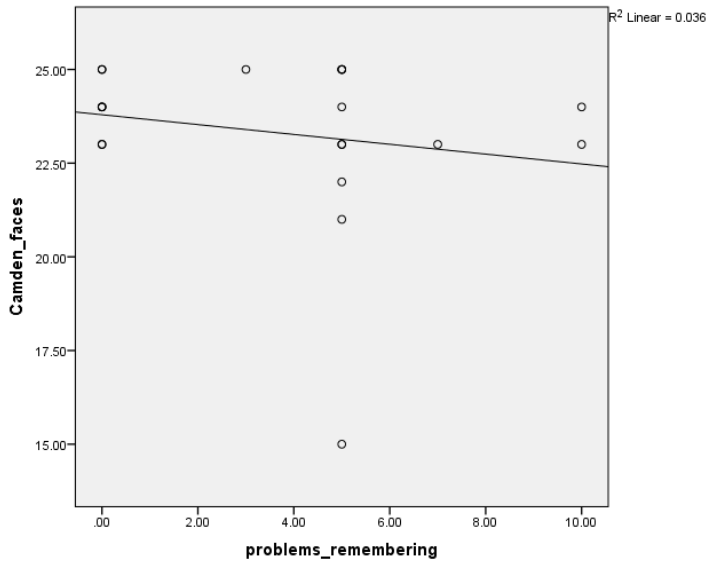
Appendix 2C: Checks for running correlational design

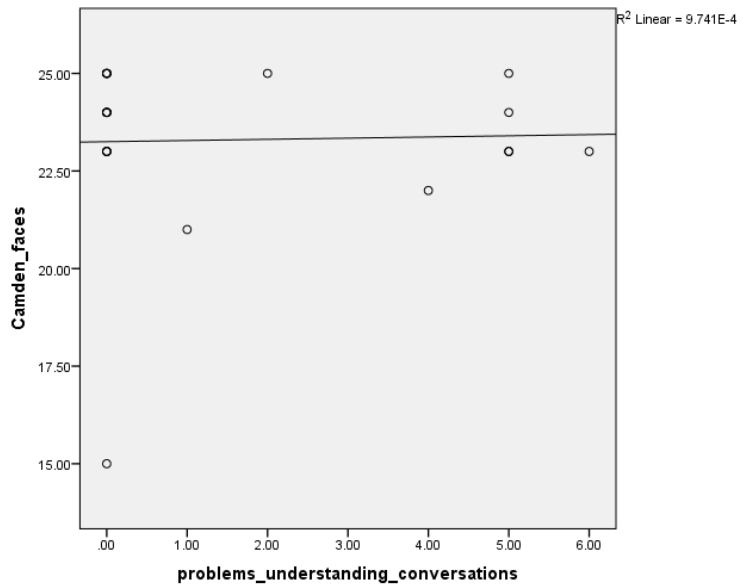




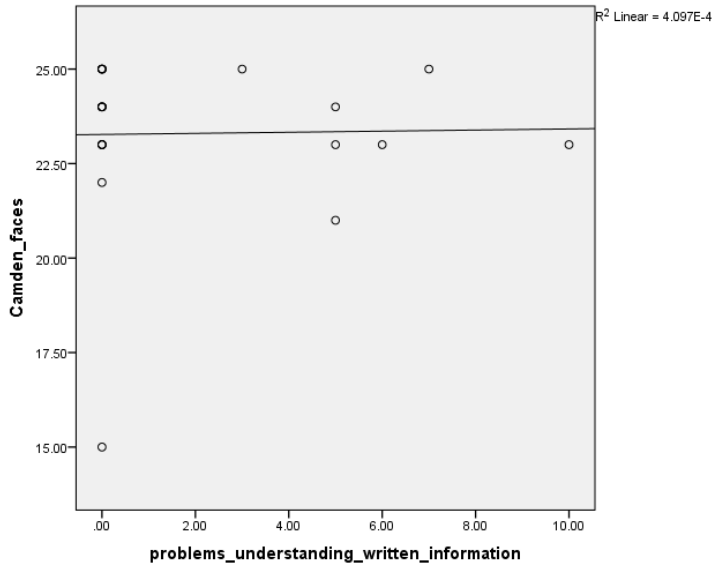
Appendix 2C: Checks for running correlational design

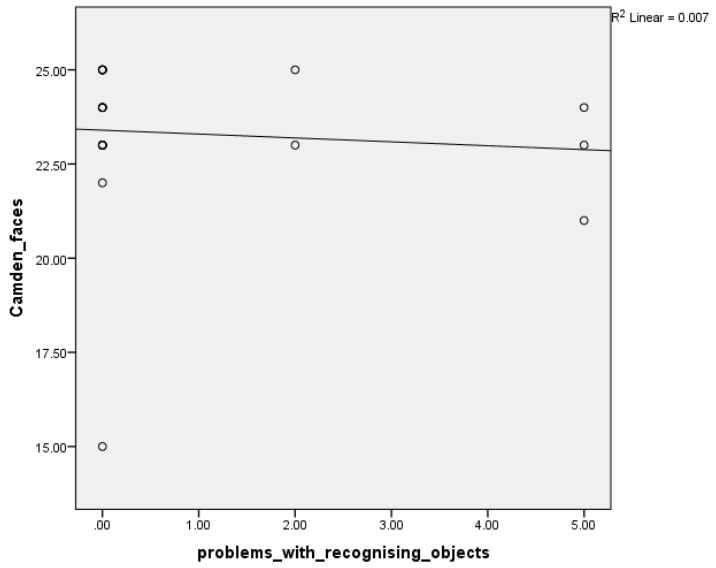
Camden Faces & Self Report measure



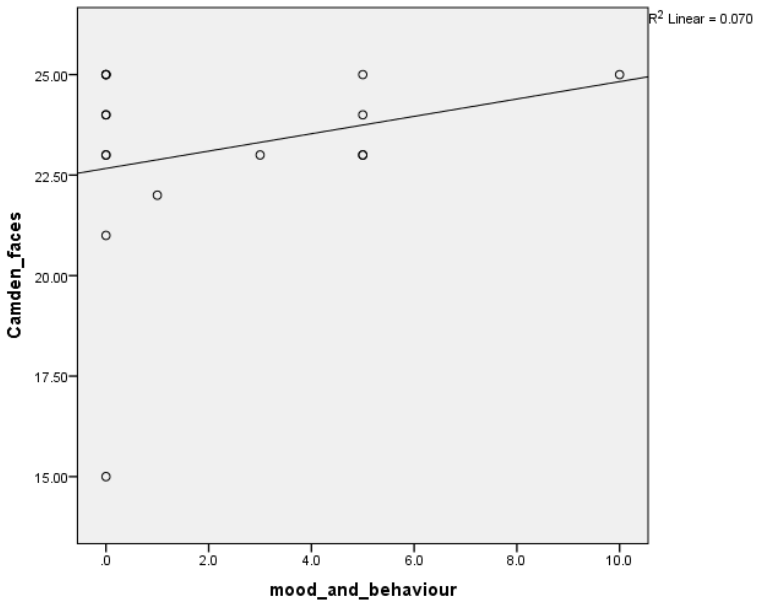


Appendix 2C: Checks for running correlational design

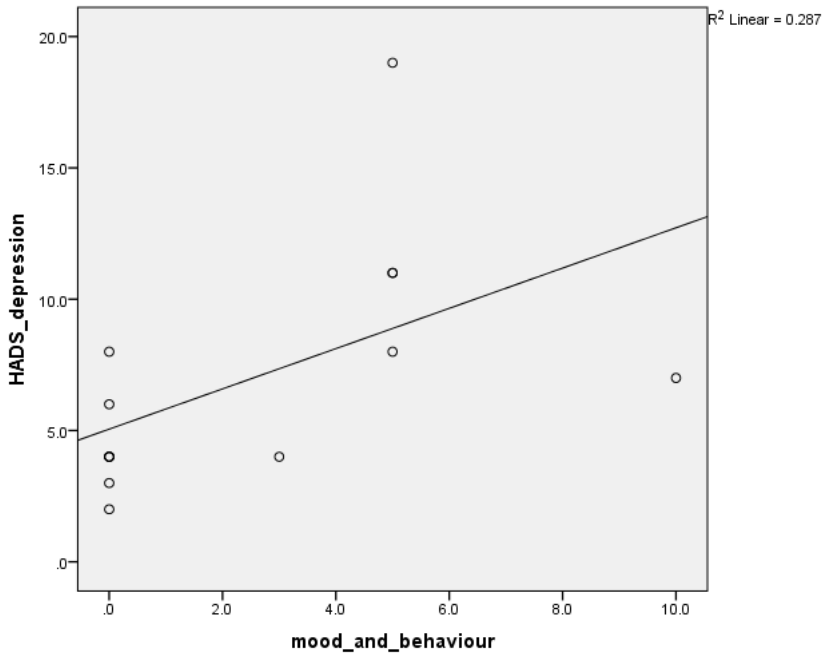




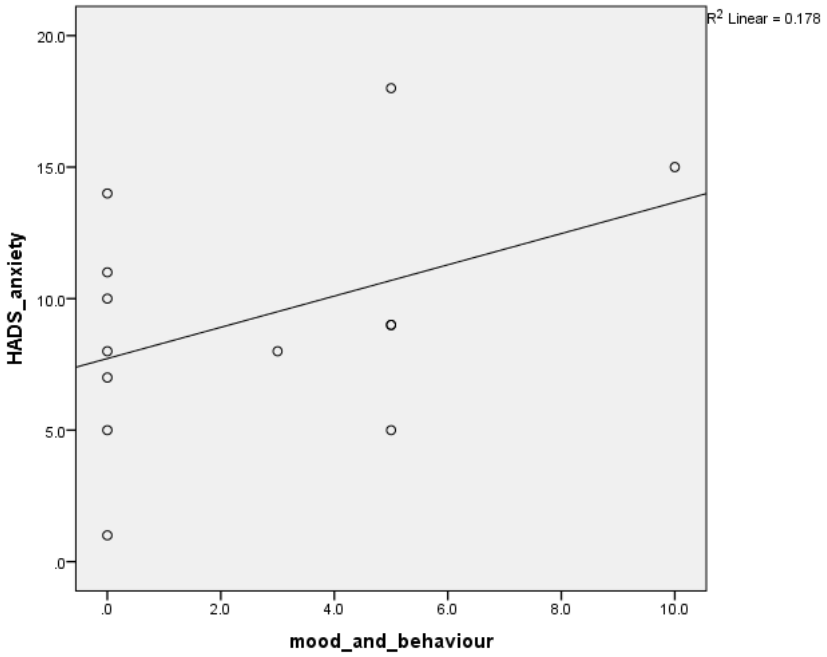
Appendix 2C: Checks for running correlational design



Baseline HADS score and self-report measure



Appendix 2C: Checks for running correlational design



Appendix 2D: Letter to chair of ethics panel at Staffordshire University

Professor David Clark-Carter

Chair of the Faculties of Health and Sciences Ethics Panel

Staffordshire University

College road

Stoke-on-Trent

Dear Professor Clark-Carter

RE: Resection in TLE; A Cognitive Profile and Perceived Cognitive Functioning in Patients with Epilepsy

Further to my thesis with Dr John Sorensen being withdrawn, I am writing to inform you that I will be carrying out my thesis with existing data from The University of Manchester. I have attached the appropriate paper work that I have been provided by my clinical supervisor (Professor Matthew Lambon-Ralph).

In my previous role at The University of Manchester I helped design and obtain funding for this study in collaboration with Professor Matthew Lambon-Ralph. I collected all the data for this piece of work and would wish to write it up as part of the thesis component of my DClinPsy. This study is part of a larger research programme at The Neuroscience Aphasia Research Unit at The University of Manchester. A proposal for this has been sent to the research director (Dr Helena Priest) and approved. I am proposing to do a comparative study looking at neuropsychological data and self-report data collected from 20 patients who have gone through Epilepsy surgery as a treatment option. I have attached my proposal as a guideline. If you have any further queries please don't hesitate to contact me.

Yours Sincerely

Sheeba Ehsan

(3rd Year Trainee Clinical Psychologist)

STAFFORDSHIRE UNIVERSITY

Appendix 2E: for response approval letter from Staffordshire University ethics panel

Faculty of Health/Faculty of Sciences

APPLICATION FOR ETHICAL APPROVAL

Student Name	Sheeba Ehsan
Date of Panel	N/A
Status of application:	Received for information

Thank you for informing the panel of the proposed changes to your research project which were received by the Faculty Ethics and IPR panel chair on 22nd February 2012.

Signed: Mark Forshaw **Date**: 28th February 2012
Chair of the Faculty of Health/Faculty of Sciences Ethics Panel

Appendix 2F: NRES Letter from Manchester

NHS

National Research Ethics Service

North West 5 Research Ethics Committee - Haydock Park
North West Centre for Research Ethics Committees
3rd Floor - Barlow House
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7819
Facsimile: 0161 237 9427

03 March 2010

Professor Matthew A Lambon Ralph
Neuroscience and Aphasia Research Unit (NARU)
School of Psychological Sciences
Zochonis Building
Oxford Road
Manchester M13 9PL

Dear Professor Lambon Ralph

Study title: **Neuropsychological investigation of memory and language problems with patients with brain damage: programme of research**
REC reference: **01/8/094**

Thank you for your letter of 23 February 2010, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair (Dr D Manning – Consultant Paediatrician).

Mental Capacity Act 2005

The members of the committee present approved the supplementary application on the basis described in the documentation submitted. I confirm that the committee has approved this research project for the purposes of the Mental Capacity Act 2005. The committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Confirmation of ethical opinion

The research continues to have a favourable opinion from this committee. It should continue to be conducted on the basis previously approved by the committee, as amended by this supplementary application. The conditions of approval issued with the committee's original favourable opinion continue to apply.

Appendix 2G: Information Sheet for Participants

Matthew A. LAMBON RALPH
Professor of Cognitive Neuroscience
Neuroscience and Aphasia Research Unit (NARU)
School of Psychological Sciences (Zochonis Building)
The University of Manchester,
Oxford Road,
Manchester M13 9PL
Tel: 0161 275 2551 (direct line)
0161 275 7348 (secretary)
Fax:0161 275 2873
Email: matt.lambon-ralph@manchester.ac.uk

Information Sheet for Participants
A STUDY INVESTIGATING LANGUAGE AND MEMORY IN PEOPLE WITH BRAIN DAMAGE.

You are being **invited** to take part in a research study. Before you decide it is important for you to **understand** why the research is being done and what it will involve.

Please **read** this information carefully and discuss it with friends and relatives. Please ask if there is anything that is **not clear** or if you would like more information.

Take time to decide whether or not you wish to take part.

What is the study about?
The aim is to **assess language** and **memory** problems in people with brain damage and to find out ways of **helping** these problems.

Why have I been chosen?
You have a **problem** with language and memory or both. Alternatively, you may have been asked to take part to provide normative data for newly developed assessments.

Do I have to take part in the study?
Taking part is **voluntary**. It is up to you whether you take part. If you do decide to take part, you will be asked to sign a **consent form**. If you decide to change your mind you are **free to withdraw** at any time and do not have to give a reason.

What will happen to me if I take part?

You will be asked to carry out some language and memory **tests**. These may use **words, pictures and symbols**. This may happen over several months but for only up to **two hours at a time.**

They will help us to gain a better understanding of these problems. They will also help us to design better tests and treatment in the future.

You can **stop** at anytime.

There are **no drugs or medical procedures** involved.

There are no risks involved. You may find that some of it will **help you**.

The experimenter will be able to **access** your **medical records.**

Will I be tape or video recorded?

Sometimes it may be helpful to **tape or video** record your answers. This might be that the researcher cannot write quickly enough or because they want to look at the answers in more detail.

Will my part in the study be kept confidential?

All information about you, both **medical and personal** will be kept **strictly confidential** by use of a coding system.

All tape recordings will be **locked away** in a cupboard by Prof. Lambon Ralph and will be used for the research only. At the end of the study all tapes will be **destroyed**.

What will happen with the results of the study?

The study will be **published** in academic and professional journals. It will also be **talked about at conferences.**

Further Questions?

If you have any further questions please contact me. My contact details are given at the top of the page.

Thank you

Version 2: 22.06.07
MREC ref: 01/8/94

Neuroscience & Aphasia Research Unit

Appendix 2H: Consent form for Participants

Matthew A. LAMBON RALPH
Professor of Cognitive Neuroscience
Neuroscience and Aphasia Research Unit (NARU)
School of Psychological Sciences (Zochonis Building)
The University of Manchester,
Oxford Road,
Manchester M13 9PL
Tel: 0161 275 2551 (direct line)
0161 275 7348 (secretary)
Fax:0161 275 2873
Email: matt.lambon-ralph@manchester.ac.uk

PARTICIPANT CONSENT FORM
A STUDY INVESTIGATING LANGUAGE AND MEMORY IN PEOPLE WITH BRAIN DAMAGE.

We would be grateful if you would **sign** this consent form.

I have **read and understand** the information sheet for the study. YES / NO
I have had the opportunity to **ask questions.** YES / NO
I have **received the answers** I need to help me make my decision. YES / NO
I understand that I am **free to with draw** from the study:

- At any time
- Without giving a reason
- Without affecting future medical care. YES / NO

I agree for my **doctor** to be informed. YES / NO
I agree for the **researcher** to have **access** to my **medical records** if necessary. YES / NO

I agree to take part in the study. YES / NO

Signed (Participant)_____

Name_____Date_____

Signed (Researcher)_____

Name_____Date_____

Version 3: 13/11/09
MREC ref: 01/8/94

Neuroscience & Aphasia Research Unit

Appendix 2I: MREC letter

Matthew A. LAMBON RALPH
Professor of Cognitive Neuroscience
Neuroscience and Aphasia Research Unit (NARU)
School of Psychological Sciences (Zochonis Building)
The University of Manchester,
Oxford Road,
Manchester M13 9PL
Tel: 0161 275 2551 (direct line)
0161 275 7348 (secretary)
Fax:0161 275 2873
Email: matt.lambon-ralph@manchester.ac.uk

13th January, 2010.

MREC: 01/8/094
Updated protocol (version 2) – to include amendments for Mental Capacity Act Section 30
Title: Neuropsychological investigation of memory and language problems with patients with brain damage: a programme of research.
PI: Prof. M.A. LAMBON RALPH

Purpose:
Our research aim is: to improve our understanding of memory and language impairments after brain damage; the neural basis of residual abilities; to improve clinical tools for diagnosis, assessment and relearning. Research involves the neuropsychological and imaging methods found in specialist clinical settings but each case is studied in greater depth. Patients are studied in detail and individually, and compared to age- and education-matched healthy participants. Data are published in international peer-reviewed journals (e.g., Brain, Neuropsychologia) either as single case-studies or case-series.

Participants:
(1) Patients with memory or language deficits after brain damage (including semantic dementia, frontotemporal dementia, Alzheimer's disease, dementia with Lewy bodies, head injury, neurosurgery, temporal lobe epilepsy, stroke, encephalitis/viral infection). Potential cases are referred by speech and language therapists, neurologists, old-age psychiatrists, other medical professions or from support groups.
(2) Healthy participants to provide control, comparative data on new assessments or imaging measures.

Consent procedure:
(1) Mental Capacity Act, Section 30: (see associated MCA1-s30 form)
Background and need of including patients without capacity: The vast majority of our patients have mild, specific impairments of memory or language, and have capacity to provide informed consent. Some patients with severe aphasia or dementia no longer have the capacity to provide informed consent. Given the purpose and aims of this study, it is important to include the fullest severity spectrum that is practicable, otherwise the research will not mirror clinical practice. With support and care, such participants are able to provide important and useful data.
Determining capacity: Either Prof. Lambon Ralph or Dr. Karen Sage will assess the ability of patients to give informed consent. Lambon Ralph is a senior neuropsychologist and a fellow of the Royal College of Speech and Language Therapists. Dr. Sage is a Senior Clinical Lecturer in Speech and Language Therapy and has over 25 years of clinical experience. In the event of any questionable cases, patients will be assessed for a second opinion by Dr. Sage if the patient was first assessed by Prof. Lambon Ralph, or by Prof. Lambon Ralph if the patient was first assessed by Dr. Sage. For patients with progressive disease, capacity will be determined on an annual basis.

by Dr. Sage. For patients with progressive disease, capacity will be determined on an annual basis.

(2) Obtaining informed consent: (for participants who are able to provide informed consent). Details of the study are provided in the information sheet. This will be provided to the patient and their carers. The nature, aims and requirements of the study will also be discussed face-to-face using aphasia-friendly materials as required. This involves discussing each section of the information sheet. Questions and queries will be actively encouraged from the patient and their carers. When the patient has had sufficient time to consider the information and discuss with careers, s/he will be asked to complete the information sheet with the researcher. Each section/question on the consent form is discussed in turn and any further queries are requested for each element.

(3) Obtaining consultee declaration: (for participants who are unable to provide consent) Details of the study are provided in the information sheet. This will be provided to the patient and their nominated consultee. The patient will always be included in the discussion and questions will be encouraged from both the patient and consultee, with the aim of involving the patient as far as possible in the decision about whether to take part in the research. The nature, aims and requirements of the study will be discussed face-to-face using aphasia-friendly materials as required. This involves discussing each section of the information sheet. Questions and queries will be actively encouraged from the patient and their consultee. When the consultee has had sufficient time to consider the information and discuss with the patient and other carers, s/he will be asked to complete the consultee declaration with the researcher. Each section/question on the consent form is discussed with the consultee and patient, and any further queries are requested for each element.

Assessment:
Patients are asked to complete a battery of neuropsychological assessments and in some cases neuroimaging investigation. The exact form of these assessments is tailored to each individual patient on the basis of their language/memory impairment. The battery is completed over a series of sessions in order to avoid fatigue. We agree the length and number of test sessions in advance with patients and their carers. We never test beyond two hours with any patient. Data collected in the project are combined with the existing clinical information (so as to avoid unnecessary duplication) and all newly-collected data are offered to referring clinicians.

Neuropsychological/aphasiological assessment: the nature of each patient's impairment and preserved skills is investigated using a battery of simple paper-and-pencil tests, or computerised equivalents. These include the following type of assessment: naming or describing a series of pictures; reading a list of words or repeating words spoken by the examiner. Sometimes we ask the patients to complete these whilst also providing a cue (e.g., DOG – "it begins with "d""). Patients are sometimes asked to point to a correct answer, given a spoken or written response. Semantic memory is also tested by asking them to match a probe item (picture, written word, etc) to an array of possible items. Other cognitive tests include their ability to recognise or recall previously-seen objects or words, and to complete assessments of memory, attention and executive, problem-solving skills (as found in most IQ test batteries), perform mental arithmetic and other calculations. Basic perceptual processes are assessed by asking the patients to make judgements about visual or auditory diagrams and stimuli. In some cases we also assess the patient's memory and language skills by asking them to try to relearn a set of items. This

typically involves repeated presentation and practice of an object's name with assistance from the examiner (e.g., through repetition of the item's name or forms of cueing).

Neuroimaging: any relevant clinical neuroimaging is collected for each patient (typically a clinical CT or sometime MRI scan). When this is missing, is no longer available, or of poor quality, we may ask the patient to undertake a neuroimaging investigation. We do not do this in all cases and so there are separate information and consent/declaration forms for the neuropsychological and neuroimaging parts of the study. The neuroimaging protocol involves MR structural scans (e.g., T1, T2, T2*, T2 flair, or DWI) and possibly a functional scan (fMRI). In both cases, participants are asked to lie in the scanner whilst images of the brain are taken. For the structural scan, the participants are asked to lie still. For the functional scan, the participants are asked to look at visually-presented stimuli or listen to words/sounds and make a response. These behavioural tasks are exactly the same as the neuropsychological assessments noted above. The scanning allows us to understand which brain parts are damaged and which are supporting the patient's remaining language and memory skills. All participants are screened with standard MRI safety questionnaires.

Data storage and analysis

All data in whatever form collected are stored in the patient's file. This is stored in a locked and dedicated filing room. Patient scans, videos and audio recordings are stored on CD, DVD and placed in the patient file. For analyses (e.g., statistical analysis of behavioural data or analyses of the MR data) anonymised data are placed onto computers. No identifiable datasets are held or stored on any computer.

Appendix 2J: First paper, Lambon Ralph et al., 2012

doi:10.1093/brain/awr325 Brain 2012: 135; 242–258 | 242

BRAIN
A JOURNAL OF NEUROLOGY

Semantic memory is impaired in patients with unilateral anterior temporal lobe resection for temporal lobe epilepsy

Matthew A. Lambon Ralph,[1] Sheeba Ehsan,[1] Gus A. Baker[2] and Timothy T. Rogers[3]

1 Neuroscience and Aphasia Research Unit (NARU), School of Psychological Sciences, University of Manchester, Manchester M13 9PL, UK
2 Walton Centre for Neurology and Neurosurgery, University of Liverpool, Liverpool L9 7LJ, UK
3 Department of Psychology, University of Madison, Madison, WI 53706-1611, USA

Correspondence to: Prof. Matthew A. Lambon Ralph,
Neuroscience and Aphasia Research Unit (NARU),
School of Psychological Sciences (Zochonis Building),
University of Manchester,
Brunswick Street,
Manchester M13 9PL, UK
E-mail: matt.lambon-ralph@manchester.ac.uk

Contemporary clinical and basic neuroscience studies have increasingly implicated the anterior temporal lobe regions, bilaterally, in the formation of coherent concepts. Mounting convergent evidence for the importance of the anterior temporal lobe in semantic memory is found in patients with bilateral anterior temporal lobe damage (e.g. semantic dementia), functional neuroimaging and repetitive transcranial magnetic stimulation studies. If this proposal is correct, then one might expect patients with anterior temporal lobe resection for long-standing temporal lobe epilepsy to be semantically impaired. Such patients, however, do not present clinically with striking comprehension deficits but with amnesia and variable anomia, leading some to conclude that semantic memory is intact in resection for temporal lobe epilepsy and thus casting doubt over the conclusions drawn from semantic dementia and linked basic neuroscience studies. Whilst there is a considerable neuropsychological literature on temporal lobe epilepsy, few studies have probed semantic memory directly, with mixed results, and none have undertaken the same type of systematic investigation of semantic processing that has been conducted with other patient groups. In this study, therefore, we investigated the semantic performance of 20 patients with resection for chronic temporal lobe epilepsy with a full battery of semantic assessments, including more sensitive measures of semantic processing. The results provide a bridge between the current clinical observations about resection for temporal lobe epilepsy and the expectations from semantic dementia and other neuroscience findings. Specifically, we found that on simple semantic tasks, the patients' accuracy fell in the normal range, with the exception that some patients with left resection for temporal lobe epilepsy had measurable anomia. Once the semantic assessments were made more challenging, by probing specific-level concepts, lower frequency/more abstract items or measuring reaction times on semantic tasks versus those on difficulty-matched non-semantic assessments, evidence of a semantic impairment was found in all individuals. We conclude by describing a unified, computationally inspired framework for capturing the variable degrees of semantic impairment found across different patient groups (semantic dementia, temporal lobe epilepsy, glioma and stroke) as well as semantic processing in neurologically intact participants.

Keywords: language processing; memory; semantic memory disorders; temporal lobe epilepsy
Abbreviations: TLE = temporal lobe epilepsy

Received August 12, 2011. Revised September 22, 2011. Accepted October 16, 2011

Introduction

Semantic memory encompasses a rich fund of general knowledge about the world, including our understanding of words, pictures, objects, sounds, faces and events (Rogers *et al.*, 2004; Jefferies and Lambon Ralph, 2006; Patterson *et al.*, 2007). It plays a critical role in many everyday verbal and non-verbal activities. Disruption of semantic memory through neurological disease or injury can, therefore, have serious consequences for patients' daily lives. The degradation of semantic memory in semantic dementia and herpes simplex encephalitis is associated with bilateral damage to and hypometabolism of the anterior temporal lobes (Nestor *et al.*, 2006; Noppeney *et al.*, 2007; Rohrer *et al.*, 2009; Mion *et al.*, 2010). Consequently, behavioural data from these patients have suggested a model in which concepts are formed through the convergence of sensory, motor and verbal experience via an anterior temporal lobe, transmodal representational hub (Rogers *et al.*, 2004), which licenses the formation of coherent concepts (Lambon Ralph *et al.*, 2010*b*).

Although previously overlooked, there is now a growing consensus that this transmodal anterior temporal lobe hub contributes critically to semantic cognition (Patterson *et al.*, 2007). This emerging view reflects a convergence of the established clinical data on semantic dementia, herpes simplex virus encephalitis, etc., with contemporary basic neuroscience studies. The multimodal, selective semantic impairment of semantic dementia can be mimicked in neurologically intact participants by applying repetitive transcranial magnetic stimulation to the lateral anterior temporal lobe (Pobric *et al.*, 2007; Lambon Ralph *et al.*, 2009; Pobric *et al.*, 2010*a*). Indeed, by applying repetitive transcranial magnetic stimulation to either the transmodal anterior temporal lobe or modality-specific information-coding regions, it is possible to probe different parts of the 'hub-and-spoke' semantic architecture (Pobric *et al.*, 2010*b*). Likewise, when using techniques that avoid (e.g. PET or magnetoencephalography) or correct for the various methodological issues associated with successful imaging of the anterior temporal lobe (Devlin *et al.*, 2000; Visser *et al.*, 2010*b*), studies find considerable bilateral anterior temporal lobe activation for multimodal semantic processing (Vandenberghe *et al.*, 1996; Marinkovic *et al.*, 2003; Sharp *et al.*, 2004; Binney *et al.*, 2010; Visser *et al.*, 2010*a*; Visser and Lambon Ralph, 2011).

The resection for temporal lobe epilepsy puzzle

Despite this considerable convergent evidence implicating an important role for the anterior temporal lobe in semantic cognition, there remains a key puzzle and potential challenge to this view. One treatment for long-standing epilepsy with focal seizures in the temporal lobe is surgical resection. In standard '*en bloc*' resection, part or all of the anterior temporal lobe (unilaterally) is removed. One example is shown in Fig. 1B. The resected area overlaps considerably with: (i) the core region of atrophy observed in semantic dementia (Fig. 1A; albeit the atrophy is bilateral, see below); (ii) the areas activated by normal participants when completing semantic tasks (example from Binney *et al.*, 2010); and (iii) the target region in our previous repetitive transcranial magnetic stimulation studies (Fig. 1C; Pobric *et al.*, 2007, 2010*b*; Lambon Ralph *et al.*, 2009). Clinically, patients with resection for temporal lobe epilepsy (TLE) do not report comprehension impairment but do complain of significant anomia and amnesia. Consequently, it is sometimes concluded that semantic processing is entirely or largely spared following resection for TLE (Hickok and Poeppel, 2004; Kho *et al.*, 2008; Simmons and Martin, 2009); a stance that could bring into question the necessity of the anterior temporal lobe in semantic cognition and could undermine the explanation of semantic impairment in semantic dementia, herpes simplex virus encephalitis, etc. This conclusion is premature, however, for three reasons:

(i) Lack of data: clinical assessment tends to focus on naming and episodic memory, and rarely on comprehension (Giovagnoli *et al.*, 2005). The same is true in the large neuropsychological published literature on TLE with and without resection. As noted above, many patients with resection for TLE complain of word-finding difficulties, which are confirmed by formal testing. The same is true in very mild semantic dementia and previous studies have demonstrated that this is driven by semantic impairment (Lambon Ralph *et al.*, 2001). It is possible, therefore, that there is measurable semantic impairment in resection for TLE but there is a dearth of studies that investigate semantic processing in the literature (see below). Consequently resection for TLE and semantic impairment might be a case of 'absence of evidence' rather than 'evidence of absence'.

(ii) Unilateral versus bilateral damage: although the affected area in resection for TLE and semantic dementia overlaps, one of the major neurological differences is that semantic dementia (as well as herpes simplex virus encephalitis, Alzheimer's disease, etc.) is a bilateral disease, whereas resection is only ever conducted unilaterally. Past investigations of semantic dementia have shown that the degree of semantic impairment is related to the extent of bilateral atrophy in this condition (Galton *et al.*, 2001; Lambon Ralph *et al.*, 2001). A previous study that compared patients with semantic dementia against those with unilateral temporal damage (of mixed aetiology including a subset of cases with resection for TLE) on the same standard semantic battery, found that unilateral damage generated minimal semantic impairment (Lambon Ralph *et al.*, 2010*a*). These results have motivated our working hypothesis that semantic memory is bilaterally distributed across left and right anterior temporal lobes. This (a) might improve the robustness of the system to damage if there is some redundancy in the bilaterally distributed representations; and (b) would give a basis for plasticity-related reorganization. Consistent with this view, recent work with computational models of a bilateral semantic system has suggested several reasons why unilateral pathology might produce dramatically less severe impairments than bilateral damage (A. C. Schapiro *et al.*, manuscript under revision).

(iii) Plasticity-related reorganization: the utility of studying resection for TLE for localization of function needs to be treated

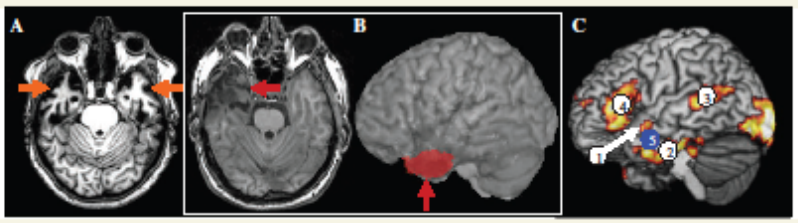


Figure 1 The puzzle of semantic memory in resection for TLE. (A) An example axial MRI for a patient with semantic dementia, with clear bilateral anterior temporal lobe atrophy (orange arrows) underpinning the patient's demonstrable semantic impairment. (B) A comparable axial slice from a patient following anterior temporal lobe unilateral resection for TLE (red arrow). The red region on the lateral view shows the resected area. This overlaps with the anterior temporal lobe regions (1 and 2 in C) activated by normal subjects in our functional MRI semantic studies (Binney *et al.*, 2010) and also with the region (5) that we have stimulated with repetitive transcranial magnetic stimulation in normal participants to produce a selective semantic effect (Pobric *et al.*, 2007; 2010; Lambon Ralph *et al.*, 2009).

with caution for various plasticity-related reasons. A long-standing seizure history complicates attempts to generalize findings from patients with resection for TLE. This point is supported by at least three findings: (a) post-operative deficits of cognition/language tend to be more severe in patients with a later age of seizure onset (Hermann *et al.*, 1999); (b) there is a significant change in the pattern of language-related white-matter pathways in patients with long-standing epilepsy (Powell *et al.*, 2007); and (c) there is significant alteration in neurotransmitter function (Hammers *et al.*, 2003). In the face of these neuroanatomical changes, semantic function may be shifted away from the seizure-related region, such that subsequent resection will have less dramatic consequences than an acute neurological event. In the limit, therefore, it is possible that resection will not produce any measurable semantic impairment because the tissue is no longer supporting this function. Secondly, after acute brain damage or neurosurgery (e.g. stroke, glioma), patients tend to demonstrate at least some degree of recovery—again suggesting a role of plasticity-related redistribution of function (Thiel *et al.*, 2001, 2005; Duffau *et al.*, 2003; Keidel *et al.*, 2010). In keeping with this notion, one early study of semantic performance in resection for TLE found a negative correlation between time post-surgery and comprehension impairment (Wilkins and Moscovitch, 1978).

As noted above, there is a considerable neuropsychological literature on the status of TLE and patients with resection for TLE but the majority of this is focused upon the patients' episodic memory impairment and on their word-finding difficulties (anomia). To date the semantic status of patients with resection for TLE has rarely been systematically assessed using the type and breadth of semantic battery that has been adopted for other patient groups (e.g. semantic dementia, herpes simplex virus encephalitis, etc.; Bozeat *et al.*, 2000; Adlam *et al.*, 2006; Lambon Ralph *et al.*, 2007). A handful of studies have assessed, however, specific aspects of semantic processing either directly or indirectly, yielding somewhat mixed results. Some studies have probed semantic memory in resection for TLE groups and found no evidence of semantic impairment on simple naming or comprehension tests (Hermann *et al.*, 1994, 1995). Most studies have found, however, evidence of anomia after resection, which is more apparent in late-onset patients with TLE (Hermann *et al.*, 1999), is more common in patients after left anterior temporal lobe resection (Martin *et al.*, 1998; Seidenberg *et al.*, 1998; Glosser *et al.*, 2003), and appears to reflect an underlying semantic weakness (Bell *et al.*, 2001; Antonucci *et al.*, 2008; Drane *et al.*, 2008). These reductions in word-finding also extend to verbal fluency tasks that have highlighted mild deficits after left or right anterior temporal lobe resection (Martin *et al.*, 1990) and have detected semantically based deficits in patients with left and right TLE prior to resection (Tröster *et al.*, 1995; N'Kaoua *et al.*, 2001). Four investigations have probed more demanding, specific-level concepts in the form of famous face recognition and naming. Glosser *et al.* (2003) found that famous face naming was impaired in both left and right TLE or patients with resection for TLE, whilst the ability to provide information about famous people became impaired after resection in the right resection for TLE subgroup alone (Glosser *et al.*, 2003). Three other studies found that patients with left TLE were impaired on famous face naming whilst cases with right TLE exhibited reduced ability in familiarity, identification and naming of famous people (Seidenberg *et al.*, 2002; Viskontas *et al.*, 2002; Drane *et al.*, 2008). Similar results were obtained in the large-scale studies reported by Tranel and colleagues (2006, 2009) whose temporal polar groups contained a majority of patients with left versus right resection for TLE. One large-scale study of (non-resected) patients with TLE probed semantic function using a multi-modal semantic battery including naming, word–picture matching and semantic association judgements and object decisions (Giovagnoli *et al.*, 2005). The investigation found that patients with left TLE scored significantly worse than controls on these measures, though the drop in performance only amounted to a few test items that would be too small a reduction to be clinically reliable at the level of individual patients. Very similar tests and results were used in a study of eight patients with left resection for TLE (Antonucci *et al.*, 2008). In addition to

the patients' anomia on confrontational naming and fluency tests, Antonucci *et al.* (2008) found evidence of a mild underlying semantic impairment by using more challenging semantic measures (semantic association judgements and synonym judgements including lower frequency and more abstract items).

The purpose of the present study was to complete the first systematic and detailed investigation of semantic memory in patients with resection for chronic TLE. Our semantic battery included various expressive and receptive tasks that have been used previously with semantic dementia, herpes simplex virus encephalitis and other patient groups (Bozeat *et al.*, 2000; Jefferies and Lambon Ralph, 2006; Lambon Ralph *et al.*, 2007, 2010a), allowing us to compare the patients with resection for TLE directly to these other neurological groups. We were mindful, however, that the standard semantic battery tests might not be sufficiently sensitive given that (i) patients with TLE and patients with resection for TLE do not present clinically with striking comprehension impairments; and (ii) a previous study of patients with unilateral temporal damage (including a subset of resection for TLE cases) did not identify major semantic impairment using typical semantic battery assessments (indicating that semantic memory might be supported in a semi-redundant fashion through bilateral temporal representation: see above and Lambon Ralph *et al.*, 2010a; A. C. Schapiro *et al.*, manuscript under revision). Accordingly, we added a set of tasks that have proved to be more sensitive to the mild semantic impairment observed in very early cases of semantic dementia (Bozeat *et al.*, 2000; Adlam *et al.*, 2006) or in neurologically intact participants after left or right lateral anterior temporal lobe repetitive transcranial magnetic stimulation (Pobric *et al.*, 2007, 2010a; Lambon Ralph *et al.*, 2009). In very early semantic dementia (like resection for TLE), patients do not necessarily complain of impaired comprehension in the clinic (on the rare occasions that they present so early) but at this stage, their semantically driven anomia is already apparent, especially on graded tests of confrontational naming (Bozeat *et al.*, 2000; Lambon Ralph *et al.*, 2001; Adlam *et al.*, 2006). Secondly, at all stages of the disease, the semantic dementia patients' semantic impairment is most apparent for concepts that are: (i) less familiar/frequent; (ii) more abstract; and (iii) more specific (Warrington, 1975; Funnell, 1995; Jefferies *et al.*, 2009; Hoffman and Lambon Ralph, 2011). As a result we probed abstract versus concrete concepts, high and low frequency words, and also the comprehension and naming of specific-level concepts (both faces and general concepts). Our previous investigations of repetitive transcranial magnetic stimulation to lateral anterior temporal lobe in neurologically intact participants confirmed this approach; repetitive transcranial magnetic stimulation has a relatively stronger effect on specific-level concepts, abstract concepts, etc. (Pobric *et al.*, 2007, 2009) and also provided another important methodological insight for the current study. Specifically, the much weaker effect of repetitive transcranial magnetic stimulation shows itself primarily through reaction times rather than reduction in accuracy, so we measured the decision/response times of patients with resection for TLE in a number of the semantic assessments. Previous repetitive transcranial magnetic stimulation studies were also useful because we had developed difficulty-matched, non-semantic decision tasks to delineate generalized slowing of reaction times from selective slowing of semantic decisions. Again, we reused the most difficult of these non-semantic, timed assessments in the present study to investigate whether any slowing of semantic performance in the patients with resection for TLE reflected general, slowed processing or a more selective semantic inefficiency. The inclusion of reaction times as well as accuracy in the current study was also prompted by one of the first systematic investigations of semantic processing in patients with resection for TLE (Wilkins and Moscovitch, 1978). These authors found that semantic performance in resection for TLE was normal if the task was conducted without time limits but scores for all patients were outside of the normal range when trial duration was limited.

Materials and methods

Patients

Twenty patients with '*en bloc*' resection for TLE (nine left and 11 right) were recruited from the epilepsy service at the Walton Centre NHS Foundation Trust (Liverpool, UK). Patients with developmental disorders, head injury, psychiatric history, stroke or glioma were excluded. Detailed background medical information for each patient is summarized in Table 1. All patients were in the chronic phase post-surgery [months post-surgery: mean = 35 (standard deviation = 19.9, min = 8)] and had long-standing epilepsy [age of diagnosis (years): mean = 13.1 (standard deviation = 10.1, min = 4)]. There was a non-significant trend for the left resection for TLE to be fewer months post-surgery than the right [left: mean = 30.3 (standard deviation = 18.6) versus right: mean = 43.0 (standard deviation = 20.6); $t(18) = 1.43$, $P = 0.17$]. Estimating from the histopathology samples, the volume of resected temporal lobe tissue varied across the cases [volume of resection (cm^3): mean = 31.9 (standard deviation = 24.2, max = 92.0)]. The patients with left and right resection for TLE had equivalent volume resection [left: mean = 28.9 cm^3 (standard deviation = 20.7) versus right: mean = 36.3 cm^3 (standard deviation = 24.0); $t(18) < 1$]. In the majority of patients, analysis of these samples revealed gliosis and neuronal loss in the hippocampal region, consistent with a diagnosis of mesial temporal sclerosis. In line with the current neuropsychological literature, all patients complained of impaired episodic memory, word-finding difficulties and significant lethargy at the end of the day. No patient reported comprehension problems, even when asked directly, and the vast majority of patients had returned to full-time work or other occupations.

Controls

The performance of patients with resection for TLE on the neuropsychological assessments was compared with the published normative data, where available. For the remaining tests and the timed assessments, their performance was compared with a group of 16 control participants. Given that the patients varied considerably across the case-series in terms of age (mean = 36.0, min = 24, max = 55 years) and education (age at leaving full-time education: mean = 18.5, min = 16, max = 22 years), there is no single obvious control group to compare them against and it would be logistically prohibitive to collect a control group for each patient. Consequently, we opted for a conservative method of comparing the patients with an older group of control participants (age: mean = 67.8, min = 62, max = 80 years;

Table 1 Background medical and biographical information

Patient	Age	Months post-surgery	Years of education	Occupation	Age at diagnosis (years)	Seizure frequency	Pre-surgical scan report	Wada language test	Post-surgery issues	Volume resected (cm^3)	Pathology report
Cases with left temporal resection											
SM	24	21	21	University student	7	Weekly+	-	-	-	55.5	Marked loss of pyramid neurons and gliosis in CA1 and CA4 plus dentate thinning; subpial gliosis in temporal neocortex
DK	49	17	18	Senior operations manager	45	Biannually	MRI: abnormal left temporal lobe—possible cavernoma	-	-	1.8	Sections show clusters of dilated vessels of varying all thickness and calibre, surrounding gliosis and haemosiderin deposition
DL	30	24	18	Accounts assistant	15	Weekly	-	-	-	68.5	Isocortex and subcortical white matter without abnormalities; hippocampal formation - extensive neuronal loss and gliosis in sector CA1 and CA2 with moderate cell loss from the dentate fascia and CA4.
AW	25	17	21	Volunteer	15	Daily	MRI: bilaterally small hippocampi	-	Subdural haematoma evacuated	20.5	Isocortex and subcortical white matter without abnormalities; other fragments cannot be identified
SS	28	8	16	Packer	15	Weekly+	-	-	Seizures came back in a cluster	32.35	Hippocampus shows focal dispersion, attenuation and loss of dentate gyrus neurons; scattered shrunken neurons and reactive astrocytes present
PW	32	60	18	-	15	Daily	MRI: reduced left hippocampal volume and high T_2 signal	Left	-	24.32	Isocortex—no diagnostic features; hippocampal formation—gliosis associated with neuronal loss, particularly of the fascia dentata
MBW	46	60	16	Machinist	22	Weekly+	MRI: reduced left hippocampal volume	-	-	16.8	Isocortex and subcortical white matter – subependymal gliosis, dystrophic calcification and ependymal canals; other fragments cannot be identified.
MF	38	30	16	Shop assistant	5	Monthly+	MRI: reduced left hippocampal volume	Left	-	24.5	Isocortex and subcortical white matter without abnormalities; hippocampal formation - neuronal loss
MM	32	36	18	Accounts assistant	13	Weekly	MRI—no significant change; contrast enhancement—signal within the hippocampal and parahippocampal gyrus; MRS-NAA ratio is slightly reduced as compared with the contralateral side	Left	Atrophy of the left temporalis nerve	16.25	Isocortex without significant abnormalities; hippocampal formation, including parts of the end of folium, fascia dentata, pyramidal cell layer with evidence of gliosis and neuronal loss
Cases with right temporal resection											
RT	24	48	22	Youth worker	10	Daily+	-	Left	-	27.64	Isocortex and subcortical white matter without evidence of dysplastic changes; hippocampus—neuronal loss and gliosis from sector CA1 and, to a lesser extent CA2, CA3 and CA4. There is marginal granule cell loss from the dentate fascia

(continued)

Table 1 Continued

Patient	Age	Months post-surgery	Years of education	Occupation	Age at diagnosis (years)	Seizure frequency	Pre-surgical scan report	Wada language test	Post-surgery issues	Volume resected (cm^3)	Pathology report
RC	55	36	21	Accountant	5	Monthly	-	-	-	55.5	Hippocampal formation—marked loss of pyramid neurons and gliosis in CA1 and CA4; thinning of dentate
JP	32	36	21	IT analyst	16	Daily +	MRI: reduced right hippocampal gyrus and high signal	Left	-	91.95	Hippocampal formation—neuronal loss and gliosis are prominent in sectors CA1 and CA3, with neuronal loss from the dentate gyrus
NA	27	74	16	Distribution centre assistant	19	Weekly +	-	Left	-	40.16	Hippocampal formation—loss and shrinkage of large pyramid neurons
MD	39	17	18	Butcher	4	Daily +	MRI: right hippocampal atrophy, particularly in anterior region	Left	Left superior quadrantinopia	52.5	Temporal lobe—normal cortex and white matter; hippocampus—neuronal loss from the regions of CA1 and CA4 with associated gliosis
LL	49	84	16	Store keeper	7	Daily +	MRI: hippocampal atrophy	Left	Left superior quadrantinopia	24.08	Hippocampal formation—severe focal loss of pyramidal neurons with corresponding gliosis; temporal lobe neocortex—no significant abnormalities; mild focal lymphocytic perivascular cuffing in neocortex and white matter
SW	21	36	16	Shop manager	8	Weekly +	MRI: right hippocampal atrophy	-	-	29.9	Temporal lobe—normal cortex and white matter; hippocampus—neuronal loss and gliosis in CA1, CA3 and CA4
CS	42	17	18	Mail line operator	17	Daily	MRI: foreign tissue lesion in the right hippocampus	Bilateral	Six months postoperative bleed	0.144	Rarefied ischaemic/post-haemorrhagic changes; no evidence of either tumour or a vascular malformation; no underlying pathological process
BB	43	48	16	Lab technician	6	Weekly	MRI: hippocampal asymmetry (right < left)	-		20.525	Hippocampus—shrinkage, increased eosinophia and loss of pyramidal neurons associated with gliosis; focal loss of neurones in the dentate gyrus
PA	28	36	21	University student	4	Daily	MRI: decreased right hippocampal volume, with increased T_2 relaxation time	Left		22.5	Isocortex, subcortical white matter—no evidence of neoplasia or dysplasia; hippocampal formation—neuronal and gliosis in sector CA1 associated with thinning of the fascia denta and mild gliosis of the end of folium
MB	32	41	16	Nursing assistant	10	Weekly +	MRI: hippocampal asymmetry right < left; hippocampal abnormalities bilaterally	Left		34.5	Isocortex and subcortical white matter—occasional focus of sclerosis with macrophages; hippocampus—extensive neuronal loss and gliosis on sectors CA1, CA3, CA4 and the dentate

Years of education = age when leaving formal education; plus sign indicates more than one event during the period noted, e.g. 'weekly+' indicates several seizures per week but less than 'daily'. MRS-NAA = magnetic resonance spectroscopy-N-acetylaspartate.

age at leaving full-time education: mean = 16.4, min = 10, max = 22 years). This choice was conservative in the sense that we could be confident that any impaired or slowed performance in the resection for TLE group was clinically significant (though it might reduce the sensitivity to subtle impairments—i.e. a type II error). As reported below, the latter potential problem did not arise (all patients were mildly impaired). In addition, for the timed synonym judgement test, we can compare the patients and older controls with the data from our previous repetitive transcranial magnetic stimulation explorations (e.g. Pobric *et al.*, 2007), which utilized exactly the same tasks. This is important because we know that vocabulary and general experience increases with age, which might boost semantic performance. The older controls mean decision times on this task were 2 s, whereas the younger repetitive transcranial magnetic stimulation participants were significantly faster in both the non-transcranial magnetic stimulation condition (1.62 s) and even after anterior temporal lobe repetitive transcranial magnetic stimulation (1.78 s), which had significantly slowed their decision times.

Assessment

The neuropsychological battery was designed to assess various aspects of general cognitive performance as well as semantic processing. Both simple and more challenging semantic assessments were included (see 'Introduction' section). Most patients were able to complete the entire battery within one or two 2-h testing sessions. In terms of general cognitive testing, we included the word and face subtests from the Camden Recognition Memory Battery (Warrington, 1996), forward and reversed digital span, copy and immediate recall of the Rey complex figure (Osterrieth, 1944) and the Raven's Coloured Progressive Matrices (Raven, 1962).

Three relatively simple semantic tasks were included to allow a direct comparison with semantic dementia. Two assessments (picture naming and spoken word–picture matching with 10 within-category choices) were drawn from the Cambridge Semantic Battery (Bozeat *et al.*, 2000). We also included a non-verbal assessment of object action-to-picture matching in which the participant is asked to select which of the three semantically related tools is used with an action demonstrated by the examiner (Bozeat *et al.*, 2002). Together, the three assessments covered verbal and non-verbal comprehension as well as simple expressive ability. All patients with mild to severe semantic dementia tend to perform below the normal range on these assessments (Bozeat *et al.*, 2000; Adlam *et al.*, 2006). Six additional, more sensitive semantic tasks were also included. Confrontational naming was assessed further through the Graded Naming Test (Warrington, 1997) and the Graded Faces Test (Thompson *et al.*, 2004) both of which contain 30 psychometrically graded items probing the ability to name less familiar general objects or famous individuals. We included this famous face assessment because it requires identification of specific-level concepts (specific individuals) and because face recognition deficits are sometimes associated with right temporal pathology.

We also administered a 96-trial synonym judgement test. This three-alternative, forced-choice task requires participants to match a probe item to one of three alternatives that are presented simultaneously in both written and spoken forms (Jefferies *et al.*, 2009). The test trials vary both frequency (high versus low) and imageability (high, medium, low) orthogonally (with 16 trials in each condition). It was a useful assessment to include in the current study for a variety of reasons: (i) it has proved to be a clinically sensitive test for semantic impairment across a variety of different patient groups (Jefferies and Lambon Ralph, 2006; Lambon Ralph *et al.*, 2007; Jefferies *et al.*, 2009); (ii) in its timed form, it is a sensitive assessment for detecting the effects of left or right lateral anterior temporal lobe repetitive transcranial magnetic stimulation in neurologically intact participants (Pobric *et al.*, 2007, 2009; Lambon Ralph *et al.*, 2009); and (iii) when used in functional MRI, it activates various regions within the anterior temporal lobe (Fig. 1C and Binney *et al.*, 2010). The resection for TLE and control participants completed the timed version of this assessment. Specifically, they were asked to indicate their choice, by way of button press, as quickly and accurately as possible. In order to assess general speed of processing on complex (non-semantic) judgements, we also administered the difficulty-matched, number-decision task from our previous repetitive transcranial magnetic stimulation explorations (Pobric *et al.*, 2007). The format of this test is the same as the synonym judgement task and participants are asked to pick which of the three alternative, double-digit numbers is closest in value to a probe number.

As an assessment of timed confrontational naming, we also asked the participants to complete a picture naming test containing 64 black and white pictures of everyday objects and animals (Lambon Ralph *et al.*, 1998*b*). The pictures were presented on a computer screen simultaneously with a beep. The participants were asked to provide the name of the picture as quickly and accurately as possible. Their responses were recorded digitally. This recording was analysed offline in order to derive both the accuracy and speed of naming. In past studies, we have found that this method allows us to collect reliable naming/reading times from patients of all severities in a much more natural manner than through the use of a voice-key trigger because participants are able to respond freely.

Our final assessments of semantic processing utilized specific-level concepts to probe the integrity of finer semantic distinctions, which tend to be vulnerable to early semantic degradation in semantic dementia (Warrington, 1975; Adlam *et al.*, 2006). Specific-level concepts from a variety of different categories were selected to ensure that the majority of normal participants were able to name and recognize each item. The picture naming version of these tests contains 22 items (each of which could be accurately named by >75% of the control participants) and the word–picture matching test contained 46 trials.

Results

The patients' performance on the general cognitive testing is summarized in Table 2. As would be expected in resection for TLE, all patients demonstrated evidence of anterograde amnesia at least for verbal materials; 19/20 patients exhibited abnormal word recognition whilst recognition memory for unfamiliar faces was within the normal range except for one patient (Patient LL). The patients generally had good forward and backward digit span (except for Patients DK, MF and BB in the forward digit span and Patients MM, BB and PA in the backwards digit span). Similarly the patients demonstrated good performance on the Rey figure copy (except for Patients MM, RC and LL) and the immediate recall of the same figure (except for Patients DL and MB). All patients exhibited excellent performance on the Raven's Coloured Progressive Matrices.

In line with the expectation derived from the current literature, the resection for TLE group's accuracy on the three simpler semantic tasks (naming, word–picture matching and object action-matching) was generally good; all patients with right resection for TLE performed in the normal range on these three

Table 2 Background neuropsychological data

	Max.	Control		Left temporal lobe resection									Right temporal lobe resection									
	score	Mean	Cut-off	SM	DK	DL	AW	SS	PW	MBW	MF	MM	RT	RC	JP	NA	MD	LL	SW	CS	BB	PA	MB
Cognitive tasks																							
Camden Recognition Memory																							
Words (percentile)	-	-	-	5	5	<5	5	5	<5	5	5	5	5	5	5	5	25	5	5	5	5	5	5
Faces (percentile)	-	-	-	90	20	75	90	50	75	75	75	75	75	90	50	90	25	5	50	90	50	75	50
Digit span: forwards	-	6.8	5	5	4	7	6	6	5	6	4	5	6	6	8	7	5	6	6	7	3	5	7
Digit span: backwards	-	4.7	2.3	4	4	5	5	6	3	5	3	2	5	4	6	3	3	4	4	4	2	2	3
Rey figure copy	36	31.03	31	36	31	31	34	34	33	35	36	30	36	26	36	36	33	23	34	31	33	36	34
Rey immediate recall	36	18.3	9	24	19	5	17	17	18	17	17	12	31	15	21	24	17	9	23	23.5	12	16	15
RCPM (percentile)	-	-	-	95	95	90	95	95	95	90	95	95	95	95	95	95	90	50	95	90	95	90	75
Semantic tasks																							
Naming	64	62.3	59.1	62	60	59	63	61	59	60	64	53	62	62	63	64	62	61	61	63	63	61	60
Word–picture matching	64	63.8	63	64	64	62	64	64	64	64	62	60	64	64	64	64	64	63	64	64	64	64	63
Object use: action-matching	36	30.2	22	33	28	29	30	29	31	31	30	13	34	32	28	33	30	28	32	28	26	29	26
Graded Faces Test	30	21.5	13.1	11	15	9	10	7	14	21	15	10	14	24	21	18	23	15	17	14	19	9	16
Graded Naming Test	30	22.1	13.5	16	17	14	13	13	10	14	13	7	16	26	22	19	21	17	21	15	16	13	14
Synonym judgement	96	94.4	92.05	86	84	84	83	80	78	74	71	69	90	90	88	88	88	87	87	86	81	79	75

RCPM = Ravens Coloured Progressive Matrices; figures in bold fall below the control cut-off.

measures. Some weakness was demonstrated by a minority of the cases with left resection for TLE (Patient DL failed naming and word–picture matching, Patient PW failed naming, Patient MF failed word–picture matching and Patient MM failed all three tasks).

In contrast, the more challenging semantic tasks revealed clear evidence for abnormality across all cases. First, on the more demanding naming tasks (Graded Naming Test, Graded Faces Test), the patients with left resection for TLE exhibited globally suppressed accuracy with 7/9 scoring below the normal cut-off on one or both tests. Replicating past studies (e.g. patients with TLE with unilateral temporal damage or left > right asymmetric semantic dementia: Martin *et al.*, 1998; Seidenberg *et al.*, 1998; Lambon Ralph *et al.*, 2001, 2010a; Glosser *et al.*, 2003), there was less pronounced anomia in the right resection cases (only Patient PA fell below the normal range). A 2 (face versus object naming) × 2 (left versus right resection) ANOVA confirmed the overall greater degree of anomia in left versus right cases [$F(1,18) = 9.88$, $P = 0.006$] but found no effect of material type [$F(1,18) < 1$] or interaction [$F(1,18) < 1$].

The 96-item synonym judgement test revealed abnormal semantic processing in all 20 patients. As can be seen in Table 1 and Fig. 2, all 20 cases fell below the control cut-off for accuracy on this test. In addition, decision times for the correct trials were also considerably and abnormally slowed: the patients' mean decision time (4.6 s) was over twice that of the older controls (1.99 s). The same pattern was found at the individual level; all except three patients' correct decision times fell outside the control range. This does not appear to reflect a generic effect or non-specific slowing; all 20 patients performed within the normal accuracy range on the difficulty-matched number decision task and 17/20 generated number decision times within the normal (older) control range.

As noted in the 'Introduction', this assessment was included in part because it contains conditions with low frequency and more abstract words, which tend to be more sensitive to the presence of semantic impairment (Jefferies *et al.*, 2009). Figure 3 confirms this pattern in the current resection for TLE group, in both accuracy and decision times. In terms of accuracy (Fig. 3), the patients only matched the control participants' performance on the easiest items (high frequency, medium or high imageability items). For the lower frequency or least imageable words, the patients' performance reduced (to 50%; per trial chance = 33%). A similar pattern was observed in the decision times for correct trials, though even on the easiest condition (high frequency, high imageability) the patients were considerably slower than the older controls. To confirm these patterns, the data were entered into a 2 (participant: patients versus controls) × 2 (frequency) × 3 (imageability) ANOVA. In terms of decision times (Fig. 3), the ANOVA confirmed a significant three-way interaction [$F(2,56) = 12.1$, $P < 0.001$]. Follow-up two-way ANOVA on each group separately found that the control group demonstrated a main effect of imageability [$F(2,18) = 86.2$, $P < 0.001$] but not of frequency [$F(1,9) = 2.03$, $P = 0.2$] or an interaction [$F(2,18) = 2.97$, $P = 0.08$], whereas the patients exhibited considerable imageability [$F(2,38) = 24.4$, $P < 0.001$] and frequency effects [$F(1,19) = 21.6$, $P < 0.001$] as well as an interaction [$F(2,38) = 24.4$, $P < 0.001$]. A very similar pattern was found for the accuracy data: there was a significant three-way interaction [group × frequency × imageability: $F(2,56) = 12.4$, $P < 0.001$], which stemmed from the control patients exhibiting an effect of imageability only [$F(2,18) = 13.7$, $P < 0.001$; frequency $F(1,9) < 1$, interaction $F(2,18) = 1.6$, $P = 0.24$]], whilst the patients were influenced substantially by both factors [frequency $F(1,19) = 30.8$, $P < 0.001$; imageability $F(2,38) = 75.7$, $P < 0.001$; interaction $F(2,38) = 34.2$, $P < 0.001$].

Given that the patients demonstrated considerably yet selectively slowed semantic performance on the synonym but not

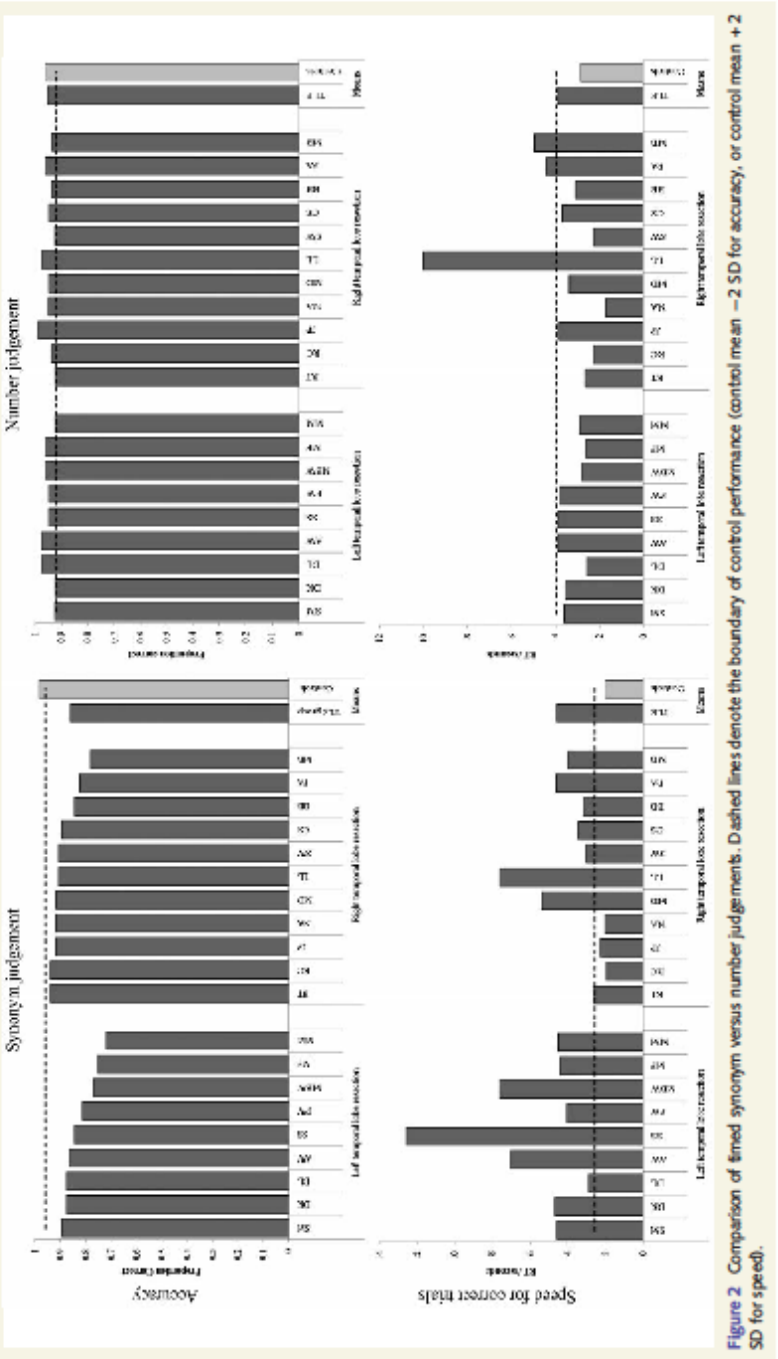


Figure 2 Comparison of timed synonym versus number judgements. Dashed lines denote the boundary of control performance (control mean −2 SD for accuracy, or control mean + 2 SD for speed).

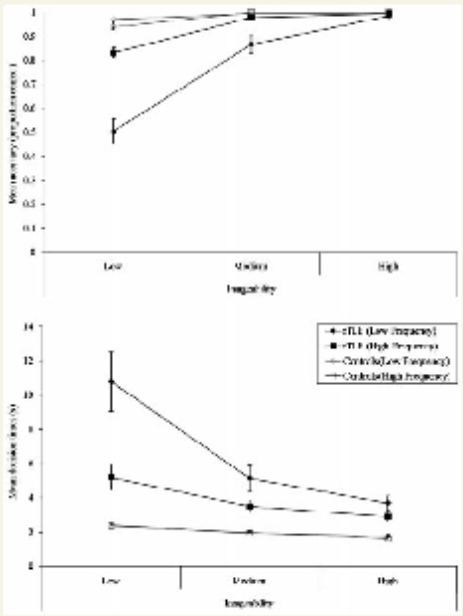


Figure 3 Influence of frequency and imageability on synonym judgement performance. rTLE = resection for TLE.

number judgement tasks (mirroring the pattern found in neurologically intact participants after left or right anterior temporal lobe repetitive transcranial magnetic stimulation: Pobric *et al.*, 2007; Lambon Ralph *et al.*, 2009), we revisited standard confrontation naming of basic-level concepts, instead measuring both accuracy and naming times (the simple naming test summarized in Table 2 used accuracy measures alone). The results are shown in Fig. 4 (accuracy in upper panel, naming speed for correct trials in lower panel). In terms of accuracy, this test replicated the earlier results (and those found in the current literature) of anomia in a minority of patients with resection for TLE (Patients SM, SS, MM and NA). In contrast, like the synonym judgement results, naming times were substantially and abnormally slow overall (mean = 2.5 s) in comparison with the older control group [mean = 1.1 s; $t(28) = 4.13$, $P < 0.001$], and abnormally slow naming times were observed in all bar three individual patients (Patients RC, NA and SW). In terms of laterality, the Graded Naming Test and Graded Faces Test assessments had revealed greater anomia in the left than right patients with resection for TLE (see above). This pattern was replicated on this basic-level naming test in terms of reaction times [left resection for TLE mean = 2.95 s (standard deviation = 1.20) versus right resection for TLE mean = 2.06 s (standard deviation = 0.63); $t(18) = 2.13$, $P = 0.05$].

The weakened semantic performance in patients with resection for TLE was also evident on the two (untimed) tests that tapped specific-level concepts. Figure 5 shows that only five individuals' accuracy in naming specific concepts fell into the normal control range (Patients SM, DL, AW, RT and RC) and, even on the receptive version of the task (word–picture matching), only half of the patients fell into the normal range (Patients SM, AW, PW, MBW, RT, RC, JP, MD, SW and BB). In summary, therefore, the semantic performance of patients with resection for TLE only appears to be 'normal' if relatively easy tasks, probing familiar concepts that use accuracy measures, are used. As soon as one of these assessment dimensions is changed (less familiar/imageable items, more specific concepts and/or reaction times) then semantic impairment in the majority, if not all, individuals is revealed.

Finally, we explored the potential relationship between the degree of semantic impairment observed (synonym judgement, speed of naming, Graded Faces Test and Graded Naming Test) in each patient and the volume of resection (Table 1). The different measures of semantic performance correlated significantly with each other across the patient case-series (synonym judgement and naming speed: $r = -0.51$, $P = 0.02$; synonym judgement and Graded Naming Test: $r = 0.77$, $P < 0.001$, Graded Faces Test and Graded Naming Test: $r = 0.50$, $P = 0.02$). If all patients were included in the analysis, none of these tests correlated with volume resected (all $P > 0.14$). There were, however, two patients [Patients DK (left) and CS (right)] who had very minimal resected volumes noted in their histopathology reports, which may have skewed the data. When these two patients were excluded from the analyses, significant correlations were found with synonym judgement accuracy ($\rho = 0.604$, $P = 0.004$ one-tailed), Graded Naming Test ($\rho = 0.606$, $P = 0.004$ one-tailed) and naming speed ($\rho = -0.401$, $P = 0.05$ one-tailed).

Discussion

The purpose of this study was to provide one of the first systematic case-series investigations of semantic processing in patients with resection for TLE. The study had both clinical and basic science motivations. The considerable accumulated database on the status of semantic memory in semantic dementia, herpes simplex virus encephalitis and other patient groups with bilateral anterior temporal lobe damage indicates a pervasive multimodal semantic impairment (Bozeat *et al.*, 2000; Coccia *et al.*, 2004; Luzzi *et al.*, 2007; Piwnica-Worms *et al.*, 2010). The conclusion that the anterior temporal lobe is a crucial component for semantic memory has been bolstered by contemporary basic neuroscience studies utilizing magnetoencephalography, distortion-corrected functional MRI, PET or repetitive transcranial magnetic stimulation (Vandenberghe *et al.*, 1996; Marinkovic *et al.*, 2003; Sharp *et al.*, 2004; Pobric *et al.*, 2007, 2010*b*; Binney *et al.*, 2010; Visser *et al.*, 2010*a*; Visser and Lambon Ralph, 2011). Despite the overlap in lesion location (Fig. 1), patients with resection for TLE generally do not complain of comprehension difficulties in the clinic but tend to note their amnesia and anomia (particularly following left temporal lobe resection). These clinical observations have led some to conclude that patients with resection for TLE do not have a semantic impairment (Hickok and Poeppel, 2004; Kho *et al.*, 2008; Simmons and Martin, 2009). The reality, however, is that the current literature contains a paucity of information

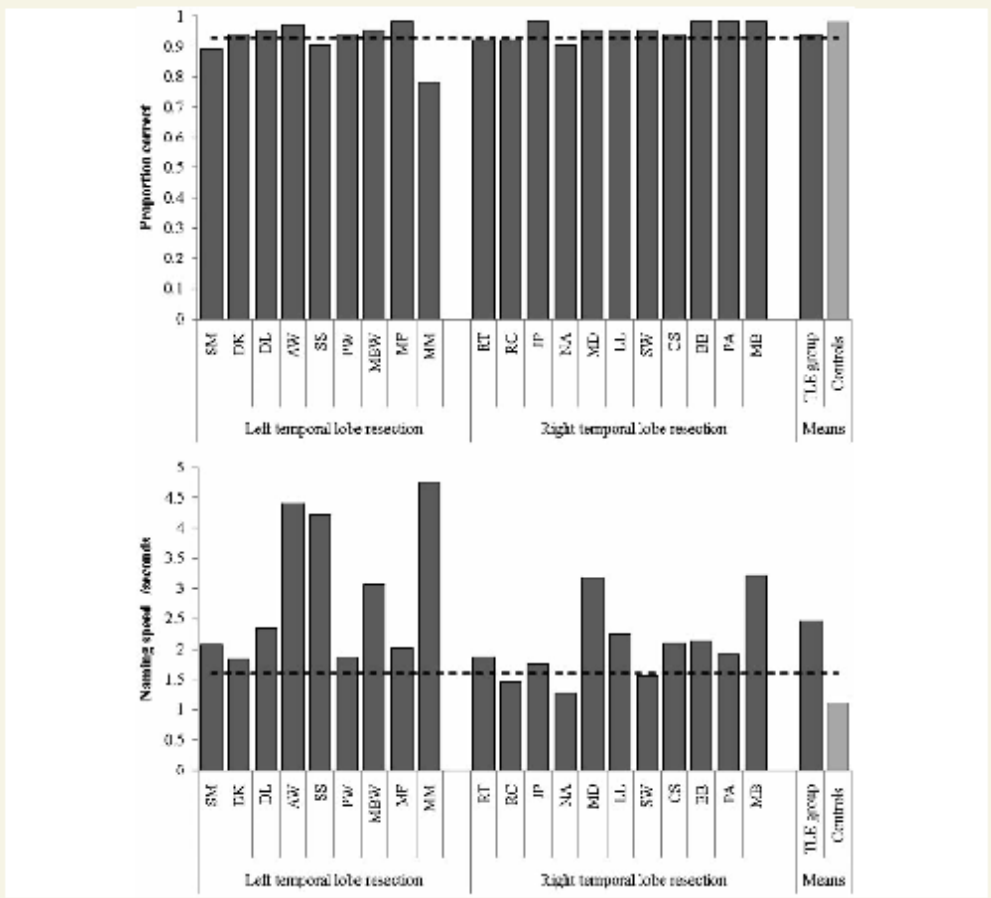


Figure 4 Performance on timed picture naming. Dashed line denotes the boundary of control performance (control mean −2 SD for accuracy, or control mean +2 SD for speed).

on the status of semantic processing in patients with TLE with or without resection and the handful of studies that have probed semantic processing using a slightly more demanding assessment (e.g. specific concepts/individuals or time-limited semantic decisions) have found indications that semantic memory may be disrupted (Wilkins and Moscovitch, 1978; Glosser *et al.*, 2003; Antonucci *et al.*, 2008). Indeed, three studies have suggested that the anomia in patients with resection for TLE may itself reflect a semantic weakness (Bell *et al.*, 2001; Antonucci *et al.*, 2008; Drane *et al.*, 2008), which would align directly with semantic dementia where the patients' profound anomia is clearly linked to the underlying degradation of conceptual knowledge (Lambon Ralph *et al.*, 2001).

The current study provides a bridge between the conclusions arising from the limited literature on semantic memory in resection for TLE and the established position for the crucial role of anterior temporal lobe in semantic processing arising from investigations of semantic dementia, herpes simplex virus encephalitis and contemporary neuroscience studies. The performance of the 20 patients with resection for TLE directly mirrors the current resection for TLE literature if we focus upon standard neuropsychological work-up, including simple clinical measures of semantic memory. Specifically, the patients present with amnesia for verbal materials, anomia in some patients (especially the cases with left resection for TLE) but no obvious comprehension impairment, through either clinical reports or formal testing. Likewise, these results also parallel investigations of patients with unilateral anterior temporal lobe damage of mixed aetiology—where naming impairment is observed following left anterior temporal lobe damage with minimal comprehension impairment (Tranel, 2009; Lambon

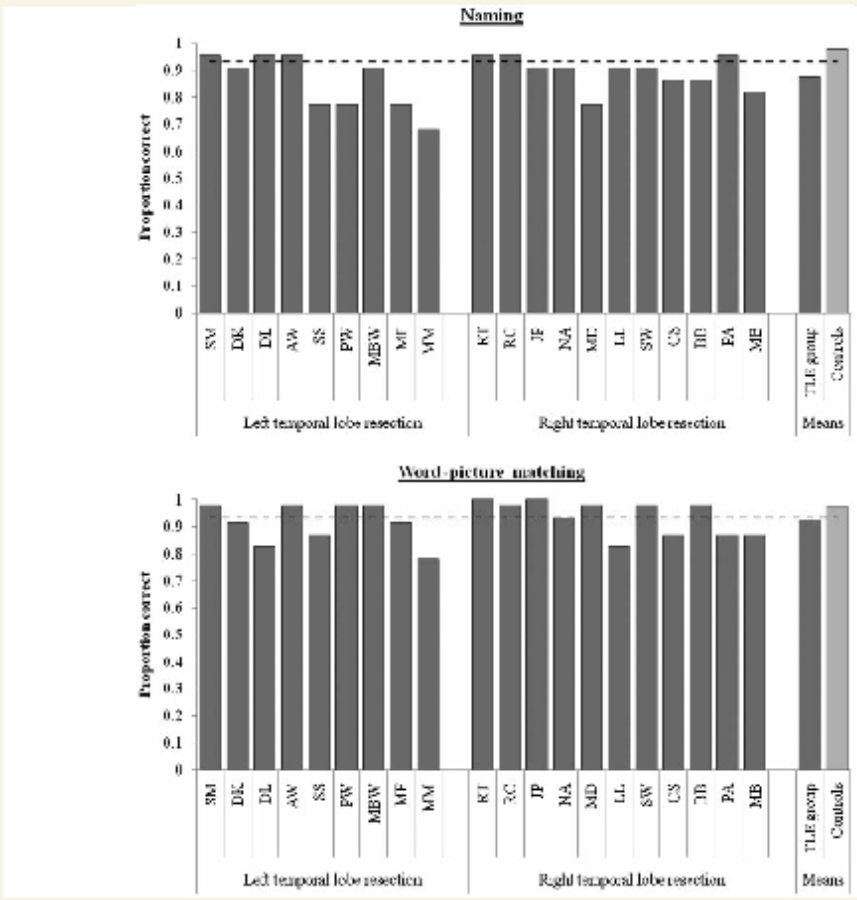


Figure 5 Performance on specific-level semantic concepts. Dashed line denotes the boundary of control performance (control mean −2 SD for accuracy, or control mean +2 SD for speed).

Ralph *et al.*, 2010a; Kemmerer *et al.*, 2011). By transferring insights from semantic dementia and repetitive transcranial magnetic stimulation investigations, it is possible to derive more targeted and sensitive assessments. This is achieved by measuring either speed of semantic processing on the more simple assessments (e.g. probing basic-level familiar concepts) or extending the materials to include less familiar, more specific or more abstract concepts. The results of these targeted semantic assessments clearly demonstrate that semantic processing is abnormal and inefficient in patients with resection for TLE, although not to the same extent as most patients with semantic dementia (see below). Specifically, even on simple basic-level, familiar concepts, the patients with resection for TLE demonstrated reaction times that were around twice that of much older control participants—an observation that replicates Wilkins and Moscovitch's (1978) finding that semantic impairment is much more apparent in time-limited tests. As soon as a semantic assessment includes more challenging materials (more specific, more abstract or less familiar) then the patients' reaction times slow even further and accuracy begins to decline—indicating that future, more sensitive clinical assessment of semantic processing in TLE/resection for TLE can be achieved by including these types of material (Antonucci *et al.*, 2008). We should note here that the slowed semantic processing in patients with resection for TLE appears to be specific to semantic cognition given that the vast majority performed within normal limits on a demanding number decision task. In fact, the data from the resection for TLE group align very closely with the selective semantic processing results found in previous studies of repetitive transcranial magnetic stimulation to left or right anterior temporal lobe (Pobric *et al.*, 2007; Lambon Ralph *et al.*, 2009).

One final, important result from the current study was that we found a significant relationship between the volume of resected tissue and resultant semantic impairment. Again this fits with the expectations arising from the clinical and basic neuroscience research on the contribution that the anterior temporal lobe makes to semantic cognition, noted above. It also replicates the similar findings from a recent study of patients with semantic impairment following temporal lobe stroke (Tsapkini *et al.*, 2011) and the relationship between the degree of bilateral anterior temporal lobe atrophy/hypometabolism and semantic impairment observed in semantic dementia (Galton *et al.*, 2001; Mion *et al.*, 2010).

We should also note that in this investigation we only studied the patients with resection for TLE post-surgery. One previous study of (non-resected) patients with TLE, which used a semantic assessment battery, found some mild semantic impairments (Giovagnoli *et al.*, 2005), suggesting that semantic performance may not be entirely normal even before resection. Given long-standing epilepsy with resultant connectivity and neurotransmitter alteration (Hammers *et al.*, 2003; Powell *et al.*, 2007), it could be possible that some or all of the patients' semantic deficit is present prior to resection because the seizure-affected part of the anterior temporal lobe system has been unable to contribute to the development of normal, detailed semantic representations, with the bulk of semantic memory being supported by the unaffected remainder of the temporal lobes, bilaterally. If correct, then the resection itself might not be the sole factor when considering the nature of semantic processing in patients with TLE with and without resection. These hypotheses could be tested in future studies by adopting the current sensitive semantic test battery in a comparison of pre- versus post-surgical patients with TLE.

We finish by considering the implications of the present findings for theories of the neural basis of semantic memory and, in particular, the role of the left and right anterior temporal lobe. Given the recent surge of studies on the anterior temporal lobe utilizing clinical and neuroscience methods, we start with a brief list of the key findings and then offer a unifying explanation for all these results, including those collected in the current study:

(i) Once various methodological issues are taken into account (Visser *et al.*, 2010*b*), functional neuroimaging studies of neurologically intact participants find bilateral, particularly inferolateral, anterior temporal lobe activation for semantic tasks across different modalities and types of concept (Vandenberghe *et al.*, 1996; Marinkovic *et al.*, 2003; Sharp *et al.*, 2004; Rogers *et al.*, 2006; Binney *et al.*, 2010; Visser *et al.*, 2010*a*; Visser and Lambon Ralph, 2011).

(ii) Patients with bilateral anterior temporal lobe pathology (e.g. semantic dementia, herpes simplex virus encephalitis, etc.) have an early and clear pan-modal semantic impairment leading to reduced accuracy on easy and hard semantic assessments unless the patients are extremely mild (Bozeat *et al.*, 2000; Adlam *et al.*, 2006). Irrespective of severity, all patients' performance is graded by frequency/familiarity, imageability and specificity (Warrington, 1975; Lambon Ralph *et al.*, 1998*a*; Jefferies *et al.*, 2009; Hoffman and Lambon Ralph, 2011).

(iii) Patients with unilateral temporal damage, even those with considerable lesions, can perform within the normal accuracy range on standard semantic battery assessments though many will show measureable anomia, especially after left temporal lobe damage and if probed with lower frequency items (Antonucci *et al.*, 2008; Tranel, 2009; Lambon Ralph *et al.*, 2010*a*; Kemmerer *et al.*, 2011; Tsapkini *et al.*, 2011).

(iv) Large-scale voxel-based lesion symptom mapping studies of stroke-related aphasic patients have demonstrated that lesions including the left superior, lateral anterior temporal lobe (centred on anterior superior temporal sulcus) are associated with the production of semantic naming errors, and that this correlation persists even when performance on challenging comprehension tests are partially out (Schwartz *et al.*, 2009; Walker *et al.*, 2011).

(v) Patients with unilateral resection for TLE can also demonstrate very good accuracy on standard semantic tasks but, if the assessments extend to more demanding concepts (along the same dimensions that affect semantic dementia performance) or probe semantic processing speed then impairments become apparent (current study; Antonucci *et al.*, 2008; Drane *et al.*, 2008). In addition, it should be noted that the level of impairment in patients with unilateral resection for TLE only matches that observed in very mild semantic dementia and is not comparable with the degree of semantic deficit observed in most patients with semantic dementia.

(vi) Neurologically intact participants show a very similar, albeit milder, pattern to the current patients with unilateral resection for TLE—namely, selective yet mild pan-modal receptive and expressive semantic processing impairments—after left or right anterior temporal lobe repetitive transcranial magnetic stimulation (measured primarily in terms of slowed reaction times: Pobric *et al.*, 2007, 2010*a*, *b*; Lambon Ralph *et al.*, 2009).

(vii) Some patients with unilateral anterior temporal lobe resection for low-grade (i.e. slow-growing) glioma can perform well on a full range of semantic tasks, even those assessed using reaction times (Campanella *et al.*, 2009; Bi *et al.*, 2011). In contrast, those with high-grade (fast-growing) tumours exhibit reduced semantic accuracy (Campanella *et al.*, 2009).

(viii) Verbal comprehension in patients with unilateral left temporal lobe lesions after stroke reflects not only the level of remaining anterior temporal lobe activation (Crinion *et al.*, 2003) and the volume of damage (Tsapkini *et al.*, 2011) but also the integrity of functional connectivity between left and right anterior temporal lobe (Warren *et al.*, 2009).

(ix) There is at least one single-case study of extensive unilateral temporal damage leading to significant multimodal semantic impairment, matching that observed in moderate semantic dementia (Patient MP: Bub *et al.*, 1988). Patient MP was initially studied for her surface dyslexia and became a standard and highly cited test case for computational models of reading. Her 'pure' surface dyslexia was accompanied by significant verbal and non-verbal semantic impairment as well as anomia (*Bub et al.*, 1988; Patterson and Behrmann, 1997). Indeed, it is intriguing that Patient MP's

set of impairments were similar to those observed in semantic dementia (multimodal semantic impairment, anomia and surface dyslexia: Patterson and Hodges, 1992; Woollams *et al.*, 2007). Whilst her data provide an important example for current consideration, the information needs to be treated with some caution in that (a) only CT scan was available; (b) her left temporal lobe damage extended to subcortical and parietal regions (Bub *et al.*, 1988; Patterson and Behrmann, 1997), and thus her semantic impairment may have been exacerbated by additional impairments of temporoparietal semantic control mechanisms (as observed in semantic aphasia: Head, 1926; Jefferies and Lambon Ralph, 2006); and (c) the damage was consequent on head injury and haematoma, which may have generated damage to other regions including the right temporal lobe.

Our working hypothesis and potential unifying explanation for this range of findings is informed by four computational models. First, the 'hub-and-spoke' model of semantic representation assumes that concepts are formed from the interaction of various modality-specific sources of information with an anterior temporal lobe transmodal representational hub (Rogers *et al.*, 2004). This representational hub allows the various sources of specific information to be distilled into coherent concepts (Patterson *et al.*, 2007; Lambon Ralph *et al.*, 2010*b*). The Rogers *et al.* (2004) model was able to demonstrate how this framework functions and, when the anterior temporal lobe hub is impaired, how the model can reproduce the pan-modal semantic impairment observed in semantic dementia. Like previous models of semantic processing (Farah and McClelland, 1991), the hub-and-spoke framework exhibited 'graceful' degradation (a non-linear relationship between amount of damage and resultant semantic impairment, such that low levels of damage generate minimal decline in accuracy on semantic tasks) and its performance under damage was modulated by intrinsic characteristics such as frequency and specificity (because the intrinsically weaker representations for low frequency and specific knowledge are less robust to the effect of damage).

Secondly, the 'no right to speak' model was, perhaps, one of the first to assume that the semantic representational hub might be functionally unitary yet underpinned by the anterior temporal lobe bilaterally (Lambon Ralph *et al.*, 2001). In addition, this model assumed that connectivity to left-lateralized speech production systems is stronger from the left anterior temporal lobe than from the right. Consequently, the degree of anomia for any level of semantic damage was much greater following left rather than right anterior temporal lobe damage. If one conceives of a hybrid of these two models, it is straightforward to imagine that a dual anterior temporal lobe hub would result in some representational redundancy between left and right components of the hub (A. C. Schapiro *et al.*, manuscript under revision). As a result, the effects of unilateral damage might be partially compensated for by the intact contralateral representational system, whereas bilateral damage might degrade both representational systems so that semantic impairment is inescapable.

The importance of connectivity patterns has been further underlined by a recent neuroanatomically constrained computational model of normal and aphasic language performance (Ueno *et al.*, 2011). Whilst retaining the insights from various computational frameworks of language, Ueno *et al.* (2011) also incorporated neuroanatomical information into the model's architecture such that it conformed to the contemporary neuroscience data in favour of dual language pathways (Parker *et al.*, 2005; Hickok and Poeppel, 2007; Saur *et al.*, 2008; Rauschecker and Scott, 2009). The model, therefore, provides a formal method for exploring the link between behaviour and neuroanatomy—licensing the simulation of aphasic data, voxel-based lesion symptom mapping results and functional neuroimaging data. Indeed, the voxel-based lesion symptom mapping data associating semantic naming errors with lesions extending to anterior superior temporal sulcus noted above (Schwartz *et al.*, 2009; Walker *et al.*, 2011) were formally simulated in this model.

The fourth and final observation from computational modelling is the demonstration that the time course of damage modulates the level of resultant impairment (Keidel *et al.*, 2010). Based on important clinical studies of low- and high-graded glioma (Thiel *et al.*, 2001, 2005; Duffau *et al.*, 2003), Keidel *et al.* (2010) investigated the behaviour of a model in which learning proceeded simultaneously with simulated damage that increased either slowly (as in low-grade glioma) or rapidly (as in high-grade glioma). With slowly increasing damage, the model compensated better for the reduction in overall computational resources. In contrast, when the same level of damage was applied much more rapidly (like high-grade glioma) or instantaneously (like stroke or other acute neurological incident) then, even with post-damage recovery/learning, the model was only able to compensate partially and never re-attained the level of performance found in the low-grade glioma simulations.

With these observations in mind, the bilateral hub-and-spoke semantic framework might account for the clinical and neuroscience findings listed above in the following manner. Under normal circumstances both anterior temporal lobe hubs work collaboratively to support pan-modal semantic processing and thus both regions are activated by neurologically intact participants in functional neuroimaging studies. Mild levels of unilateral damage/interference (transcranial magnetic stimulation) reduce the overall level of computational efficiency and thus reaction times for semantic tasks become slowed. Partial redundancy in the representational structure coded in left and right hubs means that the effects of unilateral damage can be compensated, in part, by the normal interaction with the contralateral hub. If damage is bilateral or if the connectivity between the regions has also been compromised by brain damage, then no such compensation can occur and much more dramatic impairments are observed. It seems unlikely that left and right anterior temporal lobe representations are completely redundant given that, with sufficient unilateral damage, accuracy on intrinsically more demanding concepts (low frequency, abstract, specific level) becomes impaired. These patterns are found if the damage/neural interference is instantaneous or relatively fast. In contrast, if the damage is much more gradual in form (e.g. low-grade glioma), then plasticity-related, small iterative adjustments in the remaining bilateral system can maintain 'normal' performance and resection of the infiltrated region generates no behavioural impairment.

Finally, we note that the consistent, cross-aetiology finding that left temporal damage generates much greater levels of anomia than right temporal lesions, follows for the same reasons as those noted in the original computational simulations (Lambon Ralph *et al.*, 2001). Given the greater connectivity from the left than the right anterior temporal lobe to left-lateralized speech production systems, naming ability (unlike other semantic tasks) is much more reliant upon the integrity of the left anterior temporal lobe. Thus even small levels of unilateral damage generate some degree of anomia. Because the anomia stems from damage to the semantic system, such patients are either unable to generate sufficient semantic input to drive successful speech production (thus generating omission or circumlocution errors), or they make semantically related naming errors (Antonucci *et al.*, 2008; Lambon Ralph *et al.*, 2010a). The fact that these patients often present as classical anomics (i.e. can provide good information about unnamed items) unless thoroughly tested with sensitive comprehension tests (Antonucci *et al.*, 2008) may follow, in part, from the interactive support within the dual anterior temporal lobe hub: lateral support from the intact right anterior temporal lobe hub may improve the quality of the activated semantic representation overall (thus enhancing performance on semantic tasks or generating better, partial circumlocutions) but with little improvement in naming performance because it is primarily the (damaged) left anterior temporal lobe semantic region that can innervate speech production. These computational insights also provide an explanation for the association between aphasic semantic naming errors and lesions in the left anterior superior temporal sulcus (Schwartz *et al.*, 2009; Walker *et al.*, 2011) and, when constrained by neuroanatomical information, computational models are able to reproduce these important voxel-based lesion symptom mapping results (Ueno *et al.*, 2011).

Acknowledgements

We thank all the patients and controls for their continued support of our research. We would also like to thank Argye Hillis and two anonymous reviewers for their constructive comments and suggestions on a previous version of this manuscript.

Funding

MRC programme grants (G0501632 and MR/J004146/1 to M.A.L.R.); NIH grant (R03 NS061164 to T.T.R.); Epilepsy Action (small project grant) to M.A.L.R., S.E. and G.A.B.

References

Adlam ALR, Patterson K, Rogers TT, Nestor PJ, Salmond CH, Acosta-Cabronero J, et al. Semantic dementia and fluent primary progressive aphasia: two sides of the same coin? Brain 2006; 129: 3066–80.

Antonucci SM, Beeson PM, Labiner DM, Rapcsak SZ. Lexical retrieval and semantic knowledge in patients with left inferior temporal lobe lesions. Aphasiology 2008; 22: 281–304.

Bell BD, Hermann BP, Woodard AR, Jones JE, Rutecki PA, Sheth R, et al. Object naming and semantic knowledge in temporal lobe epilepsy. Neuropsychology 2001; 15: 434–43.

Bi Y, Wei T, Wu C, Han Z, Jiang T, Caramazza A. The role of the left anterior temporal lobe in language processing revisited: evidence from an individual with ATL resection. Cortex 2011; 47: 575–87.

Binney RJ, Embleton KV, Jefferies E, Parker GJM, Lambon Ralph MA. The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: evidence from a novel direct comparison of distortion-corrected fMRI, rTMS, and semantic dementia. Cereb Cortex 2010; 20: 2728–38.

Bozeat S, Lambon Ralph MA, Patterson K, Garrard P, Hodges JR. Non-verbal semantic impairment in semantic dementia. Neuropsychologia 2000; 38: 1207–15.

Bozeat S, Lambon Ralph MA, Patterson K, Hodges JR. When objects lose their meaning: what happens to their use? Cogn Affect Behav Neurosci 2002; 2: 236–51.

Bub D, Black S, Hampson E, Kertesz A. Semantic encoding of pictures and words: some neuropsychological observations. Cogn Neuropsychol 1988; 5: 27–66.

Campanella F, Mondani M, Skrap M, Shallice T. Semantic access dysphasia resulting from left temporal lobe tumours. Brain 2009; 132: 87–102.

Coccia M, Bartolini M, Luzzi S, Provinciali L, Lambon Ralph MA. Semantic memory is an amodal, dynamic system: evidence from the interaction of naming and object use in semantic dementia. Cogn Neuropsychol 2004; 21: 513–27.

Crinion JT, Lambon Ralph MA, Warburton EA, Howard D, Wise RJS. Temporal lobe regions engaged during normal speech comprehension. Brain 2003; 126: 1193–201.

Devlin JT, Russell RP, Davis MH, Price CJ, Wilson J, Moss HE, et al. Susceptibility-induced loss of signal: comparing PET and fMRI on a semantic task. Neuroimage 2000; 11: 589–600.

Drane DL, Ojemann GA, Aylward E, Ojemann JG, Johnson LC, Silbergeld DL, et al. Category-specific naming and recognition deficits in temporal lobe epilepsy surgical patients. Neuropsychologia 2008; 46: 1242–55.

Duffau H, Capelle L, Denvil D, Sichez N, Gatignol P, Lopes M, et al. Functional recovery after surgical resection of low grade gliomas in eloquent brain: hypothesis of brain compensation. J Neurol Neurosurg Psychiatr 2003; 74: 901–7.

Farah MJ, McClelland JL. A computational model of semantic memory impairment: modality specificity and emergent category specificity. J Exper Psychol Gen 1991; 120: 339–57.

Funnell E. Objects and properties: a study of the breakdown of semantic memory. Memory 1995; 3: 497–518.

Galton CJ, Patterson K, Graham K, Lambon Ralph MA, Williams G, Antoun N, et al. Differing patterns of temporal atrophy in Alzheimer's disease and semantic dementia. Neurology 2001; 57: 216–25.

Giovagnoli AR, Erbetta A, Villani F, Avanzini G. Semantic memory in partial epilepsy: verbal and non-verbal deficits and neuroanatomical relationships. Neuropsychologia 2005; 43: 1482–92.

Glosser G, Salvucci AE, Chiaravalloti ND. Naming and recognizing famous faces in temporal lobe epilepsy. Neurology 2003; 61: 81–6.

Hammers A, Koepp MJ, Richardson MP, Hurlemann R, Brooks DJ, Duncan JS. Grey and white matter flumazenil binding in neocortical epilepsy with normal MRI. A PET study of 44 patients. Brain 2003; 126: 1300–18.

Head H. Aphasia and kindred disorders of speech. London: Cambridge University Press; 1926.

Hermann B, Davies K, Foley K, Bell B. Visual confrontation naming outcome after standard left anterior temporal lobectomy with sparing versus resection of the superior temporal gyrus: a randomized prospective clinical trial. Epilepsia 1999; 40: 1070–6.

Hermann BP, Seidenberg M, Haltiner A, Wyler AR. Relationship of age at onset, chronologic age, and adequacy of preoperative performance to

verbal memory change after anterior temporal lobectomy. Epilepsia 1995; 36: 137–45.
Hermann BP, Wyler AR, Somes G, Dohan FC, Berry AD, Clement L, et al. Declarative memory following anterior temporal lobectomy in humans. Behav Neurosci 1994; 108: 3–10.
Hickok G, Poeppel D. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 2004; 92: 67–99.
Hickok G, Poeppel D. The cortical organization of speech processing. Nat Rev Neurosci 2007; 8: 393–402.
Hoffman P, Lambon Ralph MA. Reverse concreteness effects are not a typical feature of semantic dementia: evidence for the hub-and-spoke model of conceptual representation. Cereb Cortex 2011. Advance Access published on February 1, 2011, doi:10.1093/cercor/bhq288.
Jefferies E, Lambon Ralph MA. Semantic impairment in stroke aphasia versus semantic dementia: a case-series comparison. Brain 2006; 129: 2132–47.
Jefferies E, Patterson K, Jones RW, Lambon Ralph MA. Comprehension of concrete and abstract words in semantic dementia. Neuropsychology 2009; 23: 492–9.
Keidel JL, Welbourne SR, Lambon Ralph MA. Solving the paradox of the equipotential and modular brain: a neurocomputational model of stroke vs. slow-growing glioma. Neuropsychologia 2010; 48: 1716–24.
Kemmerer D, Rudrauf D, Manzel K, Tranel D. Behavioral patterns and lesion sites associated with impaired processing of lexical and conceptual knowledge of actions. Cortex 2011. Advance Access published on December 16, 2010, doi:10.1016/j.cortex.2010.11.001.
Kho KH, Indefrey P, Hagoort P, van Veelen CWM, van Rijen PC, Ramsey NF. Unimpaired sentence comprehension after anterior temporal cortex resection. Neuropsychologia 2008; 46: 1170–8.
Lambon Ralph MA, Cipolotti L, Manes F, Patterson K. Taking both sides: do unilateral anterior temporal lobe lesions disrupt semantic memory? Brain 2010a; 133: 3243–55.
Lambon Ralph MA, Graham KS, Ellis AW, Hodges JR. Naming in semantic dementia - what matters? Neuropsychologia 1998a; 36: 775–84.
Lambon Ralph MA, Howard D, Nightingale G, Ellis AW. Are living and non-living category-specific deficits causally linked to impaired perceptual or associative knowledge? Evidence from a category-specific double dissociation. Neurocase 1998b; 4: 311–38.
Lambon Ralph MA, Lowe C, Rogers TT. Neural basis of category-specific semantic deficits for living things: evidence from semantic dementia, HSVE and a neural network model. Brain 2007; 130: 1127–37.
Lambon Ralph MA, McClelland JL, Patterson K, Galton CJ, Hodges JR. No right to speak? The relationship between object naming and semantic impairment: neuropsychological abstract evidence and a computational model. J Cogn Neurosci 2001; 13: 341–56.
Lambon Ralph MA, Pobric G, Jefferies E. Conceptual knowledge is underpinned by the temporal pole bilaterally: convergent evidence from rTMS. Cereb Cortex 2009; 19: 832–8.
Lambon Ralph MA, Sage K, Jones RW, Mayberry EJ. Coherent concepts are computed in the anterior temporal lobes. Proc Natl Acad Sci USA 2010b; 107: 2717–22.
Luzzi S, Snowden JS, Neary D, Coccia M, Provinciali L, Lambon Ralph MA. Distinct patterns of olfactory impairment in Alzheimer's disease, semantic dementia, frontotemporal dementia, and corticobasal degeneration. Neuropsychologia 2007; 45: 1823–31.
Marinkovic K, Dhond RP, Dale AM, Glessner M, Carr V, Halgren E. Spatiotemporal dynamics of modality-specific and supramodal word processing. Neuron 2003; 38: 487–97.
Martin RC, Loring DW, Meador KJ, Lee GP. The effects of lateralized temporal lobe dysfunction on normal and semantic word fluency. Neuropsychologia 1990; 28: 823–9.
Martin RC, Sawrie SM, Roth DL, Gilliam FG, Faught E, Morawetz RB, et al. Individual memory change after anterior temporal lobectomy: a base rate analysis using regression-based outcome methodology. Epilepsia 1998; 39: 1075–82.
Mion M, Patterson K, Acosta-Cabronero J, Pengas G, Izquierdo-Garcia D, Hong YT, et al. What the left and right anterior fusiform gyri tell us about semantic memory. Brain 2010; 133: 3256–68.
N'Kaoua B, Lespinet V, Barsse A, Rougier A, Claverie B. Exploration of hemispheric specialization and lexico-semantic processing in unilateral temporal lobe epilepsy with verbal fluency tasks. Neuropsychologia 2001; 39: 635–42.
Nestor PJ, Fryer TD, Hodges JR. Declarative memory impairments in Alzheimer's disease and semantic dementia. Neuroimage 2006; 30: 1010–20.
Noppeney U, Patterson K, Tyler LK, Moss H, Stamatakis EA, Bright P, et al. Temporal lobe lesions and semantic impairment: a comparison of herpes simplex virus encephalitis and semantic dementia. Brain 2007; 130: 1138–47.
Osterrieth P. Le test de copie d'une figure complexe. Arch Psychologie 1944; 30: 205–550.
Parker GJM, Luzzi S, Alexander DC, Wheeler-Kingshott CAM, Ciccarelli O, Lambon Ralph MA. Non-invasive structural mapping of two auditory-language pathways in the human brain. Neuroimage 2005; 24: 656–66.
Patterson K, Behrmann M. Frequency and consistency effects in a pure surface dyslexic patient. J Exper Psychol: Hum Percept Perform 1997; 23: 1217–31.
Patterson K, Hodges JR. Deterioration of word meaning: implications for reading. Neuropsychologia 1992; 30: 1025–40.
Patterson K, Nestor PJ, Rogers TT. Where do you know what you know? The representation of semantic knowledge in the human brain. Nat Rev Neurosci 2007; 8: 976–87.
Piwnica-Worms KE, Omar R, Hailstone JC, Warren JD. Flavour processing in semantic dementia. Cortex 2010; 46: 761–8.
Pobric G, Jefferies E, Lambon Ralph MA. Amodal semantic representations depend on both anterior temporal lobes: evidence from repetitive transcranial magnetic stimulation. Neuropsychologia 2010a; 48: 1336–42.
Pobric G, Jefferies E, Lambon Ralph MA. Category-specific versus category-general semantic impairment induced by transcranial magnetic stimulation. Curr Biol 2010b; 20: 964–8.
Pobric G, Lambon Ralph MA, Jefferies E. The role of the anterior temporal lobes in the comprehension of concrete and abstract words: rTMS evidence. Cortex 2009; 45: 1104–10.
Pobric GG, Jefferies E, Lambon Ralph MA. Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. Proc Natl Acad Sci USA 2007; 104: 20137–41.
Powell HWR, Parker GJM, Alexander DC, Symms MR, Boulby PA, Wheeler-Kingshott CAM, et al. Abnormalities of language networks in temporal lobe epilepsy. Neuroimage 2007; 36: 209–21.
Rauschecker JP, Scott SK. Maps and streams in the auditory cortex: nonhuman primates illuminate human speech processing. Nat Neurosci 2009; 12: 718–24.
Raven JC. Coloured progressive matrices: sets A, AB, B. London: HK Lewis; 1962.
Rogers TT, Hocking J, Noppeney U, Mechelli A, Gorno-Tempini ML, Patterson K, et al. Anterior temporal cortex and semantic memory: reconciling findings from neuropsychology and functional imaging. Cogn Affect Behav Neurosci 2006; 6: 201–13.
Rogers TT, Lambon Ralph MA, Garrard P, Bozeat S, McClelland JL, Hodges JR, et al. The structure and deterioration of semantic memory: a neuropsychological and computational investigation. Psychol Rev 2004; 111: 205–35.
Rohrer JD, Warren JD, Modat M, Ridgway GR, Douiri A, Rossor MN, et al. Patterns of cortical thinning in the language variants of frontotemporal lobar degeneration. Neurology 2009; 72: 1562–9.
Saur D, Kreher BW, Schnell S, Kümmerer D, Kellmeyer P, Vry M-S, et al. Ventral and dorsal pathways for language. Proc Natl Acad Sci USA 2008; 105: 18035–40.
Schwartz MF, Kimberg DY, Walker GM, Faseyitan O, Brecher A, Dell GS, et al. Anterior temporal involvement in semantic word retrieval:

voxel-based lesion-symptom mapping evidence from aphasia. Brain 2009; 132: 3411–27.
Seidenberg M, Griffith R, Sabsevitz D, Moran M, Haltiner A, Bell B, et al. Recognition and identification of famous faces in patients with unilateral temporal lobe epilepsy. Neuropsychologia 2002; 40: 446–56.
Seidenberg M, Hermann B, Wyler AR, Davies K, Dohan FC, Leveroni C. Neuropsychological outcome following anterior temporal lobectomy in patients with and without the syndrome of mesial temporal lobe epilepsy. Neuropsychology 1998; 12: 303–16.
Sharp DJ, Scott SK, Wise RJS. Retrieving meaning after temporal lobe infarction: the role of the basal language area. Ann Neurol 2004; 56: 836–46.
Simmons WK, Martin A. The anterior temporal lobes and the functional architecture of semantic memory. J Int Neuropsychol Soc 2009; 15: 645–9.
Thiel A, Habedank B, Winhuisen L, Herholz K, Kessler J, Haupt WF, et al. Essential language function of the right hemisphere in brain tumor patients. Ann Neurol 2005; 57: 128–31.
Thiel A, Herholz K, Koyuncu A, Ghaemi M, Kracht LW, Habedank B, et al. Plasticity of language networks in patients with brain tumors: a positron emission tomography activation study. Ann Neurol 2001; 50: 620–9.
Thompson SA, Graham KS, Williams G, Patterson K, Kapur N, Hodges JR. Dissociating person-specific from general semantic knowledge: roles of the left and right temporal lobes. Neuropsychologia 2004; 42: 359–70.
Tranel D. Impaired naming of unique landmarks is associated with left temporal polar damage. Neuropsychology 2006; 20: 1–10.
Tranel D. The left temporal pole is important for retrieving words for unique concrete entities. Aphasiology 2009; 23: 867–84.
Tröster AI, Warmflash V, Osorio I, Paolo AM, Alexander LJ, Barr WB. The roles of semantic networks and search efficiency in verbal fluency performance in intractable temporal lobe epilepsy. Epilepsy Res 1995; 21: 19–26.
Tsapkini K, Frangakis CE, Hillis AE. The function of the left anterior temporal pole: evidence from acute stroke and infarct volume. Brain 2011; 134: 3094–3105.
Ueno T, Saito S, Rogers TT, Lambon Ralph MA. Lichtheim 2: synthesising aphasia and the neural basis of language in a neurocomputational model of the dual dorsal-ventral language pathways. Neuron 2011; 72: 385–96.
Vandenberghe R, Price C, Wise R, Josephs O, Frackowiak RSJ. Functional-anatomy of a common semantic system for words and pictures. Nature 1996; 383: 254–6.
Visiontas IV, McAndrews MP, Moscovitch M. Memory for famous people in patients with unilateral temporal lobe epilepsy and excisions. Neuropsychology 2002; 16: 472–80.
Visser M, Embleton KV, Jefferies E, Parker GJ, Lambon Ralph MA. The inferior, anterior temporal lobes and semantic memory clarified: novel evidence from distortion-corrected fMRI. Neuropsychologia 2010a; 48: 1689–96.
Visser M, Jefferies E, Lambon Ralph MA. Semantic processing in the anterior temporal lobes: a meta-analysis of the functional neuroimaging literature. J Cogn Neurosci 2010b; 22: 1083–94.
Visser M, Lambon Ralph MA. Differential contributions of bilateral ventral anterior temporal lobe and left anterior superior temporal gyrus to semantic processes. J Cogn Neurosci 2011; 23: 3121–31.
Walker GM, Schwartz MF, Kimberg DY, Faseyitan O, Brecher A, Dell GS, et al. Support for anterior temporal involvement in semantic error production in aphasia: new evidence from VLSM. Brain Lang 2011; 117: 110–22.
Warren JE, Crinion JT, Lambon Ralph MA, Wise RJS. Anterior temporal lobe connectivity correlates with functional outcome after aphasic stroke. Brain 2009; 132: 3428–42.
Warrington EK. The selective impairment of semantic memory. Q J Exper Psychol 1975; 27: 635–57.
Warrington EK. Short Recognition Memory Test. Hove: Psychology Press; 1996.
Warrington EK. The Graded Naming Test: a restandardisation. Neuropsychol Rehabil 1997; 7: 143–6.
Wilkins A, Moscovitch M. Selective impairment of semantic memory after temporal lobectomy. Neuropsychologia 1978; 16: 73–9.
Woollams AM, Lambon Ralph MA, Plaut DC, Patterson K. SD-squared: on the association between semantic dementia and surface dyslexia. Psychol Rev 2007; 114: 316–39.

Appendix 2K. Journal guidelines for Epilepsy & Behaviour

Epilepsy & Behaviour

EPILEPSY RESEARCH

AUTHOR INFORMATION PACK

TABLE OF CONTENTS

ISSN: 0920-1211

DESCRIPTION

Epilepsy Research provides for publication of high quality articles in both experimental and clinical **epilepsy** research, with a special emphasis on translational research that ultimately relates to epilepsy as a human condition. The journal is intended to provide a forum for reporting the best and most rigorous **epilepsy research** from all disciplines ranging from **biophysics** and **molecular biology** to **epidemiological** and **psychosocial** research. As such the journal will publish original papers relevant to epilepsy from any scientific discipline and also studies of a multidisciplinary nature. Clinical and experimental research papers adopting fresh conceptual approaches to the study of epilepsy and its treatment are encouraged. The overriding criteria for publication are novelty, significant clinical or experimental relevance, and interest to a multidisciplinary audience in the broad arena of epilepsy. Review articles focused on any topic of epilepsy research will also be considered, but only if they present an exceptionally clear synthesis of current knowledge and future directions of a research area, based on a critical assessment of the available data or on hypotheses that are likely to stimulate more critical thinking and further advances in an area of epilepsy research.

Benefits to authors
We also provide many author benefits, such as free PDFs, a liberal copyright policy, special discounts on Elsevier publications and much more. Please click here for more information on our author services.

Please see our Guide for Authors for information on article submission. If you require any further information or help, please visit our support pages: http://support.elsevier.com

AUDIENCE

Epileptologists, neurologists, clinical neurophysiologists, pharmacologists, psychiatrists.

IMPACT FACTOR

2013: 2.190 © Thomson Reuters Journal Citation Reports 2014

ABSTRACTING AND INDEXING

Elsevier BIOBASE
Chemical Abstracts
Current Contents/Life Sciences
MEDLINE®
EMBASE
Reference Update
Science Citation Index
Scopus

EDITORIAL BOARD

GUIDE FOR AUTHORS

Types of article

The journal will publish full-length original articles, full-length feature reviews or mini-reviews and short communications. In general, it the policy of Epilepsy Research to not publish case reports. Our focus is on the publication of hypothesis driven empirical quantitative research data. Letters to the Editor will be published at the Editors discretion.

Every effort will be made to notify authors about acceptance or rejection within 4 to 6 weeks. Categories of manuscripts include:
1) Full-length Papers: giving findings of original basic or clinical research in any area of epilepsy within the scope of the journal.

2) Short Communications: 1,500 words plus no more than 3 figures or tables in total 20 references.

3) Review Articles: on specialised topics within the scope of the journal. Prospective authors should contact the Editor-in-Chief or one of the Associate Editors beforehand.

Language (usage and editing services)
Please see the section below for full details here.

BEFORE YOU BEGIN

Ethics in publishing

For information on Ethics in publishing and Ethical guidelines for journal publication see http://www.elsevier.com/publishingethics and http://www.elsevier.com/journal-authors/ethics.

Human and animal rights

If the work involves the use of animal or human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans http://www.wma.net/en/30publications/10policies/b3/index.html; EU Directive 2010/63/EU for animal experiments http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm; Uniform Requirements for manuscripts submitted to Biomedical journals http://www.icmje.org. Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

Conflict of interest

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/ registrations, and grants or other funding. See also http://www.elsevier.com/conflictsofinterest. Further information and an example of a Conflict of Interest form can be found at: http://help.elsevier.com/app/answers/detail/a_id/286/p/7923.

Submission declaration and verification

Submission of an article implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis or as an electronic preprint, see http://www.elsevier.com/postingpolicy), that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder. To verify originality, your article may be checked by the originality detection service CrossCheck http://www.elsevier.com/editors/plagdetect.

Changes to authorship

This policy concerns the addition, deletion, or rearrangement of author names in the authorship of accepted manuscripts:
Before the accepted manuscript is published in an online issue: Requests to add or remove an author, or to rearrange the author names, must be sent to the Journal Manager from the corresponding author of the accepted manuscript and must include: (a) the reason the name should be added or removed, or the author names rearranged and (b) written confirmation (e-mail, fax, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors,

this includes confirmation from the author being added or removed. Requests that are not sent by the corresponding author will be forwarded by the Journal Manager to the corresponding author, who must follow the procedure as described above. Note that: (1) Journal Managers will inform the Journal Editors of any such requests and (2) publication of the accepted manuscript in an online issue is suspended until authorship has been agreed.
After the accepted manuscript is published in an online issue: Any requests to add, delete, or rearrange author names in an article published in an online issue will follow the same policies as noted above and result in a corrigendum.

Article transfer service

This journal is part of our Article Transfer Service. This means that if the Editor feels your article is more suitable in one of our other participating journals, then you may be asked to consider transferring the article to one of those. If you agree, your article will be transferred automatically on your behalf with no need to reformat. More information about this can be found here: http://www.elsevier.com/authors/article-transfer-service.

Copyright

This journal offers authors a choice in publishing their research: Open access and Subscription.

For subscription articles
Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' (for more information on this and copyright, see http://www.elsevier.com/copyright). An e-mail will be sent to the corresponding author confirming receipt of the manuscript together with a 'Journal Publishing Agreement' form or a link to the online version of this agreement.
Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution and for all other derivative works, including compilations and translations (please consult http://www.elsevier.com/permissions). If excerpts from other copyrighted works are included, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has preprinted forms for use by authors in these cases: please consult http://www.elsevier.com/permissions.

For open access articles
Upon acceptance of an article, authors will be asked to complete an 'Exclusive License Agreement' (for more information see http://www.elsevier.com/OAauthoragreement). Permitted reuse of open access articles is determined by the author's choice of user license (see http://www.elsevier.com/openaccesslicenses).

Retained author rights
As an author you (or your employer or institution) retain certain rights. For more information on author rights for:
Subscription articles please see http://www.elsevier.com/journal-authors/author-rights-and-responsibilities.
Open access articles please see http://www.elsevier.com/OAauthoragreement.

Role of the funding source

You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should be stated.

Funding body agreements and policies

Elsevier has established agreements and developed policies to allow authors whose articles appear in journals published by Elsevier, to comply with potential manuscript archiving requirements as specified as conditions of their grant awards. To learn more about existing agreements and policies please visit http://www.elsevier.com/fundingbodies.

Open access

This journal offers authors a choice in publishing their research:

Open access

• Articles are freely available to both subscribers and the wider public with permitted reuse
• A open access publication fee is payable by authors or their research funder

Subscription

• Articles are made available to subscribers as well as developing countries and patient groups through our access programs (http://www.elsevier.com/access)
• No open access publication fee

All articles published open access will be immediately and permanently free for everyone to read and download. Permitted reuse is defined by your choice of one of the following Creative Commons user licenses:

Creative Commons Attribution-NonCommercial-ShareAlike (CC BY-NC-SA): for non-commercial purposes, lets others distribute and copy the article, to create extracts, abstracts and other revised versions, adaptations or derivative works of or from an article (such as a translation), to include in a collective work (such as an anthology), to text and data mine the article, as long as they credit the author(s), do not represent the author as endorsing their adaptation of the article, do not modify the article in such a way as to damage the author's honor or reputation, and license their new adaptations or creations under identical terms (CC BY-NC-SA).

Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND): for non-commercial purposes, lets others distribute and copy the article, and to include in a collective work (such as an anthology), as long as they credit the author(s) and provided they do not alter or modify the article.

Elsevier has established agreements with funding bodies, http://www.elsevier.com/fundingbodies. This ensures authors can comply with funding body open access requirements, including specific user licenses, such as CC BY. Some authors may also be reimbursed for associated publication fees. If you need to comply with your funding body policy, you can apply for the CC BY license after your manuscript is accepted for publication.

To provide open access, this journal has a publication fee which needs to be met by the authors or their research funders for each article published open access.
Your publication choice will have no effect on the peer review process or acceptance of submitted articles.

The open access publication fee for this journal is **$2500**, excluding taxes. Learn more about Elsevier's pricing policy: http://www.elsevier.com/openaccesspricing.

Language (usage and editing services)

Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible grammatical or spelling errors and to conform to correct scientific English may wish to use the English Language Editing service available from Elsevier's WebShop (http://webshop.elsevier.com/languageediting/) or visit our customer support site (http://support.elsevier.com) for more information.

Submission

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts source files to a single PDF file of the article, which is used in the peer-review process. Please note that even though manuscript source files are converted to PDF files at submission for the review process, these source files are needed for further processing after acceptance. All correspondence, including notification of the Editor's decision and requests for revision, takes place by e-mail removing the need for a paper trail.

Please submit your article via http://ees.elsevier.com/epires

PREPARATION

Use of word processing software

It is important that the file be saved in the native format of the word processor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do not use the word processor's options to justify text or to hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns.

The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier: http://www.elsevier.com/guidepublication). Note that source files of figures, tables and text graphics will be required whether or not you embed your figures in the text. See also the section on Electronic artwork.
To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

Subdivision - numbered sections
Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

Introduction
State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

Material and methods
Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.

Results
Results should be clear and concise.

Discussion
This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

Conclusions
The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

Appendices
If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

- ***Title.*** Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.
- ***Author names and affiliations.*** Where the family name may be ambiguous (e.g., a double name), please indicate this clearly. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.
- ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. **Ensure that phone numbers (with country and area code) are provided in addition to the e-mail address and the complete postal address. Contact details must be kept up to date by the corresponding author.**
- ***Present/permanent address.*** If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

Graphical abstract

A Graphical abstract is optional and should summarize the contents of the article in a concise, pictorial form designed to capture the attention of a wide readership online. Authors must provide images that clearly represent the work described in the article. Graphical abstracts should be submitted as a separate file in the online submission system. Image size: Please provide an image with a minimum of 531 × 1328 pixels (h × w) or proportionally more. The image should be readable at a size of 5 × 13 cm using a regular screen resolution of 96 dpi. Preferred file types: TIFF, EPS, PDF or MS Office files. See http://www.elsevier.com/graphicalabstracts for examples.
Authors can make use of Elsevier's Illustration and Enhancement service to ensure the best presentation of their images also in accordance with all technical requirements: Illustration Service.

Highlights

Highlights are mandatory for this journal. They consist of a short collection of bullet points that convey the core findings of the article and should be submitted in a separate file in the online submission system. Please use 'Highlights' in the file name and include 3 to 5 bullet points (maximum 85 characters, including spaces, per bullet point). See http://www.elsevier.com/highlights for examples.

Keywords

Immediately after the abstract, provide a maximum of 6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

Abbreviations

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

Units

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

Math formulae

Present simple formulae in the line of normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. In principle, variables are to be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Footnotes

Footnotes should be used sparingly. Number them consecutively throughout the article, using superscript Arabic numbers. Many wordprocessors build footnotes into the text, and this feature may be used. Should this not be the case, indicate the position of footnotes in the text and present the footnotes themselves separately at the end of the article. Do not include footnotes in the Reference list.

Table footnotes

Indicate each footnote in a table with a superscript lowercase letter.

Electronic artwork

General points

- Make sure you use uniform lettering and sizing of your original artwork.
- Embed the used fonts if the application provides that option.
- Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.
- Number the illustrations according to their sequence in the text.
- Use a logical naming convention for your artwork files.
- Provide captions to illustrations separately.
- Size the illustrations close to the desired dimensions of the printed version.
- Submit each illustration as a separate file.

A detailed guide on electronic artwork is available on our website:
http://www.elsevier.com/artworkinstructions
You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format.
Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):
EPS (or PDF): Vector drawings, embed all used fonts.
TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.
TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.
TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.

Please do not:

- Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
- Supply files that are too low in resolution;
- Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color on the Web (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. **For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article**. Please indicate your preference for color: in print or on the Web only. For further information on the preparation of electronic artwork, please see http://www.elsevier.com/artworkinstructions.
Please note: Because of technical complications which can arise by converting color figures to 'gray scale' (for the printed version should you not opt for color in print) please submit in addition usable black and white versions of all the color illustrations.

Figure captions

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Tables

Number tables consecutively in accordance with their appearance in the text. Place footnotes to tables below the table body and indicate them with superscript lowercase letters. Avoid vertical rules. Be sparing in the use of tables and ensure that the data presented in tables do not duplicate results described elsewhere in the article.

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Web references

As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

References in a special issue

Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.

Reference style

Text: All citations in the text should refer to:

1. *Single author:* the author's name (without initials, unless there is ambiguity) and the year of publication;
2. *Two authors:* both authors' names and the year of publication;
3. *Three or more authors:* first author's name followed by 'et al.' and the year of publication.

Citations may be made directly (or parenthetically). Groups of references should be listed first alphabetically, then chronologically.

Examples: 'as demonstrated (Allan, 2000a, 2000b, 1999; Allan and Jones, 1999). Kramer et al. (2010) have recently shown ....'

List: References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.

Examples:

Reference to a journal publication:

Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2010. The art of writing a scientific article. J. Sci. Commun. 163, 51–59.

Reference to a book:

Strunk Jr., W., White, E.B., 2000. The Elements of Style, fourth ed. Longman, New York.

Reference to a chapter in an edited book:

Mettam, G.R., Adams, L.B., 2009. How to prepare an electronic version of your article, in: Jones, B.S., Smith , R.Z. (Eds.), Introduction to the Electronic Age. E-Publishing Inc., New York, pp. 281–304.

Journal abbreviations source

Journal names should be abbreviated according to the List of Title Word Abbreviations: http://www.issn.org/services/online-services/access-to-the-ltwa/.

Video data

Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the files in one of our recommended file formats with a preferred maximum size of 50 MB. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages at http://www.elsevier.com/artworkinstructions. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

AudioSlides

The journal encourages authors to create an AudioSlides presentation with their published article. AudioSlides are brief, webinar-style presentations that are shown next to the online article on ScienceDirect. This gives authors the opportunity to summarize their research in their own words and to help readers understand what the paper is about. More information and examples are available at http://www.elsevier.com/audioslides. Authors of this journal will automatically receive an invitation e-mail to create an AudioSlides presentation after acceptance of their paper.

Supplementary data

Elsevier accepts electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, high-resolution images, background datasets, sound clips and more. Supplementary files supplied will be published online alongside the electronic version of your article in Elsevier Web products, including ScienceDirect: http://www.sciencedirect.com. In order to ensure that your submitted material is directly usable, please provide the data in one of our recommended file formats. Authors should submit the material in electronic format together with the article and supply a concise and descriptive caption for each file. For more detailed instructions please visit our artwork instruction pages at http://www.elsevier.com/artworkinstructions.

3D neuroimaging

You can enrich your online articles by providing 3D neuroimaging data in NIfTI format. This will be visualized for readers using the interactive viewer embedded within your article, and will enable them to: browse through available neuroimaging datasets; zoom, rotate and pan the 3D brain reconstruction; cut through the volume; change opacity and color mapping; switch between 3D and 2D projected views; and download the data. The viewer supports both single (.nii) and dual (.hdr and .img) NIfTI file formats. Recommended size of a single uncompressed dataset is 100 MB or less. Multiple datasets can be submitted. Each dataset will have to be zipped and uploaded to the online submission system via the '3D neuroimaging data' submission category. Please provide a short informative description for each dataset by filling in the 'Description' field when uploading a dataset. Note: all datasets will be available for downloading from the online article on ScienceDirect. If you have concerns about your data being downloadable, please provide a video instead. For more information see: http://www.elsevier.com/3DNeuroimaging.

Submission checklist

The following list will be useful during the final checking of an article prior to sending it to the journal for review. Please consult this Guide for Authors for further details of any item.

Ensure that the following items are present:

One author has been designated as the corresponding author with contact details:

- E-mail address
- Full postal address
- Phone numbers

All necessary files have been uploaded, and contain:

- Keywords
- All figure captions
- All tables (including title, description, footnotes)

Further considerations

- Manuscript has been 'spell-checked' and 'grammar-checked'
- References are in the correct format for this journal
- All references mentioned in the Reference list are cited in the text, and vice versa
- Permission has been obtained for use of copyrighted material from other sources (including the Web)
- Color figures are clearly marked as being intended for color reproduction on the Web (free of charge) and in print, or to be reproduced in color on the Web (free of charge) and in black-and-white in print
- If only color on the Web is required, black-and-white versions of the figures are also supplied for printing purposes

For any further information please visit our customer support site at http://support.elsevier.com.

AFTER ACCEPTANCE

Use of the Digital Object Identifier

The Digital Object Identifier (DOI) may be used to cite and link to electronic documents. The DOI consists of a unique alpha-numeric character string which is assigned to a document by the publisher upon the initial electronic publication. The assigned DOI never changes. Therefore, it is an ideal medium for citing a document, particularly 'Articles in press' because they have not yet received their full bibliographic information. Example of a correctly given DOI (in URL format; here an article in the journal *Physics Letters B*):

http://dx.doi.org/10.1016/j.physletb.2010.09.059

When you use a DOI to create links to documents on the web, the DOIs are guaranteed never to change.

Online proof correction

Corresponding authors will receive an e-mail with a link to our online proofing system, allowing annotation and correction of proofs online. The environment is similar to MS Word: in addition to editing text, you can also comment on figures/tables and answer questions from the Copy Editor. Web-based proofing provides a faster and less error-prone process by allowing you to directly type your corrections, eliminating the potential introduction of errors.

If preferred, you can still choose to annotate and upload your edits on the PDF version. All instructions for proofing will be given in the e-mail we send to authors, including alternative methods to the online version and PDF.

We will do everything possible to get your article published quickly and accurately - please upload all of your corrections within 48 hours. It is important to ensure that all corrections are sent back to us in one communication. Please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility. Note that Elsevier may proceed with the publication of your article if no response is received.

Offprints

The corresponding author, at no cost, will be provided with a PDF file of the article via e-mail (the PDF file is a watermarked version of the published article and includes a cover sheet with the journal cover image and a disclaimer outlining the terms and conditions of use). For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's WebShop (http://webshop.elsevier.com/myarticleservices/offprints). Authors requiring printed copies of multiple articles may use Elsevier WebShop's 'Create Your Own Book' service to collate multiple articles within a single cover (http://webshop.elsevier.com/myarticleservices/booklets).

AUTHOR INQUIRIES

You can track your submitted article at http://help.elsevier.com/app/answers/detail/a_id/89/p/8045/. You can track your accepted article at http://www.elsevier.com/trackarticle. You are also welcome to contact Customer Support via http://support.elsevier.com.

Paper 3: A reflexive review on thesis writing

Word count: 2745

Abstract

This paper presents an account of the valuable experiences gained throughout the process of completing a piece of research for the Doctorate in Clinical Psychology. The first paper within this thesis is a systematic review of studies investigating semantic memory (SM) problems in post-resection temporal lobe epilepsy patients. The second paper reports an empirical investigation into SM problems in this client group using standardised and self-report measures. Valuable learning experiences are highlighted in this paper. An exploration of process and reflective issues will also be offered throughout.

1.0 Introduction

In this thesis three papers are presented. Paper 1 summarises the systematic search for, and review of, studies examining the effects of surgical intervention for semantic memory (SM) in adults with temporal lobe epilepsy (TLE). Paper 2 provides an empirical report of an investigation into SM impairment using standardised neuropsychological (objective) and self-report (subjective) measures. This final paper offers a first-person reflective account of the process of completing this thesis and of writing the literature review and research report papers.

1.1. The development of my interests in neuropsychology

I have always been interested in the interplay between brain and behaviour and psychology as a means of understanding. Whilst studying for a degree in psychology, my introduction to the discipline of cognitive neuroscience, which aims to understand how "brain function gives rise to mental activity" (Kosslyn & Shinn., 1992, p.146), was instrumental. During this period I volunteered in a stroke rehabilitation ward with a dedicated clinical neuropsychologist. During my experience as a volunteer, I learnt about the significance of clinical neuropsychology in relation to its aims of assessment and rehabilitation of people with altered function as a result of brain injury and illness trauma. I realised how brain injury infiltrates thorough to behaviour and emotion, and the impact of this on individuals and their families. I have since gained experience working in a research capacity with some very prominent and passionate people in the area who have encouraged my journey.

As a trainee clinical psychologist, I have worked with various clients with a range of neurological presentations and associated deficits that can be highly debilitating and distressing. These experiences have fostered my interest in how psychological knowledge can be drawn on to assess and rehabilitate people.

2.0. Selecting a research project

The process of selecting a research topic for the doctorate thesis (DClinPsy) is never straightforward. For me, this journey began with a research project in bipolar disorder and validating a psycho-educational tool. I will share my experience of NHS ethical committees and the research and development process before my third year at which point this thesis became no longer feasible for various reasons and as a result my research path changed.

2.1. Developing as a researcher

Initially I met with a project supervisor who was teaching on the DClinPsy. I agreed to commence a project that would require recruitment of individuals with bipolar disorder in order to validate an interview tool. I felt that conducting such a study would clinically benefit clients by providing psycho-education and consequently raising awareness regarding their disorder. University peer review approval was obtained and an application for NHS ethical approval was submitted online, via the National Research Ethics Service (NRES). I was invited to an ethics panel review meeting to answer questions about the research, which led to suggestions being made and approval being granted (Appendix 3a). Further to this, I submitted my project to the local NHS Trust for Research and Development (R & D) approval. On reflection, I did not anticipate this stage of the process requiring the length of time which ensued. The unpredictability generated a sense of 'feeling out of control' as a student. An update meeting was arranged with my clinical supervisor, at which I was advised that the project was no longer feasible, due to time commitments. Perturbed by the whole situation, I contacted the DClinPsy department and shared my concerns. Following this, I arranged a meeting with my research colleagues in Manchester with whom I had worked as a researcher prior to my clinical doctorate; this led to a discussion regarding data that was already available for analysis. I then embarked on a thesis attached to my original interest in neuropsychology.

Thinking through the available options, I realised that working with existing data had a number of benefits at this stage. Not having to collect data would have pragmatic advantages, given the short-time scale that was ahead. Specifically, I thought about my contribution to the dataset that I was planning to utilise. My

contribution in my research role had been from study design to grant application, all the way through to data collection, analysis and write up, subsequent to which I commenced the clinical doctorate. The data represented the field of neuropsychology with a population of epilepsy surgery patients. This research would provide a learning opportunity on working with data representing a unique clinical group.

2.2. Developing the research idea

My situation dictated my thesis options and my research idea was a by-product of my predicament. I had been instrumental in the conception of the research idea in a conversation with my then supervisor, however this was prior to commencing the DClinPsy. In a way this assisted me to rationalise working with an existing data set, which was an option that I had not previously considered.

I was curious about the broader research programme at The University of Manchester which was assessing language and memory, specifically SM, across patient groups. I had seen a variety of clinical presentations in my role which involved assessing cognition using standardised and novel neuropsychological test batteries. On reflection, my clinical intuition at the time highlighted that patients often reported different impairments to those highlighted on standardised tests. For example, patients may report that they found certain items difficult or disagreed with results of neuropsychological tests. A conversation at the time with my research colleague at Manchester University led to a question around self-report versus standardised assessment in SM. At the time, these conversations had led to developing a self-report questionnaire measure of SM, which was used alongside the standardised neuropsychological test battery (subjective versus objective measures). During my doctorate, I reflected on this experience and discussed this with my academic supervisor and research director on the DClinPsy. This led to my decision to work with existing data comparing SM via questionnaire (subjective) and neuropsychological test (objective) data, in individuals who have undergone unilateral temporal lobe epilepsy (TLE) resection.

3.0. The choice of a literature review topic

Following consultation with my academic course supervisor, I realised that it would be necessary to find out more about SM in TLE surgery patients. I was aware of the course requirements of producing work of a publishable standard. My supervisor suggested that I carry out a systematic review, a process that would pose many learning opportunities and challenges. Firstly I familiarised myself with this area of research and the process of systematic review. I had some prior experience which was enhanced by using training available at the library and within the NHS. I found no literature reviews on SM post resection in TLE. I realised this would be a good opportunity to fill this gap.

Initially having a broad research focus provided me with information which was vital for me to understand TLE. What was striking was the disparity in measurement of aspects of SM (through expressive and receptive language measures). A broad scooping exercise enabled a more focused review by allowing me to reflect on my reading and my experience of the field. A key piece of research formed an integral part of the research report (Lambon Ralph, Ehsan, Baker & Rogers, 2012); this paper uses the same dataset that my thesis later utilised. I was aware that as I am a co-author with my previous supervisor on this paper; this would mean reviewing my own paper as part of the review process. I pondered on some of the challenges this may present, and not having previous experience of this, accepted that this was an important learning point. I discussed this with my current academic supervisor who was encouraging and was instrumental in assisting me to be objective in my review.

3.1. Literature review critique

The literature review was not without challenges; because I already had my data available, I had made some assumptions regarding the research area. However, I felt that this assisted me to take a more methodical and meticulous approach with assistance from my supervisor. One of the key strengths of the literature review was that it was conducted in accordance with guidelines for systematic reviews, making it replicable (Cochrane Collaboration, 2011). This

helped to focus my thinking around defining the review question and also developing criteria for the inclusion of studies. On reflection, in order to shift my thinking from a mental health project and to embrace the new study question, I searched multiple resources such as published and unpublished work. This both assisted me to adjust to my thesis topic and formed a crucial step in the review process.

A limitation of the review and perhaps inevitable in research is the variation in study designs brought together. I was disappointed by this; however I knew that I was limited by the findings of the review.

4.0. Critical appraisal of empirical research study

4.1. Design

The design of the original study was a case series design, described as an observational study reporting on data from a select group, without a comparison population (Gordis, 2004). This was a key strength of this dataset as it enabled a select group, with characteristics of interest, undergoing a novel treatment, to be followed up. A key advantage of a case series design is that it is thought to be a feasible design requiring fewer resources than, for example, randomised controlled trials (Bhandari & Joensson, 2009).

4.2. Interview questionnaire

Working with a data set meant that I was required to find out more about the measures utilised in the original study. I decided to find out more about people with epilepsy; fortunately, I was on placement in a neuropsychology department. I learnt that a key challenge for neuropsychologists working with individuals with epilepsy is the measurement of cognitive functioning. My clinical experience has demonstrated that there can be fluctuations in function caused by seizure experience, however even healthy people can also have a certain number of low scores when large test batteries are used. The questionnaire from which I retrieved data, was semi structured, including open ended questions with a rating scale. Developing a questionnaire requires conceptualisation of the construct to be measured, and test validity is often a challenge faced when developing novel

measures. Self-report can be seen as a measure of what the person wishes the researcher to know, and this can be influenced by many factors. Construct validity via self-report of a 'real' variable such as SM is not well established and poses a challenge.

4.3. Procedure

Even though I worked with an existing dataset, I was aware from the original data collection that the study procedure placed significant demands on the participants and the researcher. The test battery which subsequently resulted in the first published paper (Lambon Ralph, Ehsan, Baker & Rogers, 2012) required testing durations of up to four hours over two sessions, and fatigue may have impacted on individual performance levels.

4.4. Sample

On reflection, a group of resected TLE patients are a unique population, as surgery is only appropriate for individuals for whom drugs have failed and/or whose seizures originate from a localised area of the brain (amounting to approximately 3% of those who develop epilepsy) (All Party Parliamentary Group on Epilepsy, 2007). This presents its own challenges for this research, as obtaining a larger sample size would require a multi-centre study on a national level which would have larger costs. However, the current study was under-powered and this was reflected in the findings.

4.5. Analysis

The data analysis chosen for this research was correlational analysis, which was appropriate given the research question (David Clark-Carter, 2010). The research aim was to explore whether self-report (subjective) SM problems of post-surgery TLE patients are associated with their performance on neuropsychological test (objective) performance. The questionnaire data was also analysed using content analysis in order to compare right and left surgery, and also explore any other themes important to participants in their post-surgery adjustment.

5.0. Reflections on working with existing data

Although there were advantages of working with existing data for my clinical thesis, it was difficult to reacquaint myself with data that I had previously collected. The process of research can be viewed as a journey in which one is immersed from start to finish, and any gaps in this process can cause a feeling of detachment. This was difficult and frustrating at times as I was required to spend significant lengths of time reviewing and re-reviewing my data. Supervision was beneficial in understanding and exploring my own skills and self-belief in this process.

6.0. Research implications and applications

The findings of this piece of research have implications for the clinical practice of clinical psychologists working with epilepsy patients. The literature review also has research implications, as it has highlighted an area of insufficient research and perhaps a discrepancy in the ways in which patients are clinically assessed for SM. One ethical implication to arise from this piece of work is that using tests which are widely available yet not sensitive may not allow clinicians to fully inform patients of cognitive risks pre-surgery. My understanding of this study is that, firstly, various neuropsychological tests are available and used clinically, and it is important that these are validated and standardised. However, it is equally important for tests to have strong ecological validity. Self-report measures of memory are less utilised, which is perhaps due to availability. Secondly, problems outside of the focus of memory are very much present post-surgery, including mood and adjustment issues which would also impact on memory. Naming tests appear to provide a good measure of SM and there are a number of published tests available, including the Graded Naming Test (GNT) (Warrington, 1980) and the Boston Naming Test (BNT) (Kaplan, Goodglass & Weintraub, 1983). However, it was The 64 Naming Test from The Cambridge Semantic Battery (Bozeat et al., 2000) that provided most relevance to self-reported problems. The BNT and GNT

are tests that have been used over many years, and my clinical reflection would be that they are perhaps used out of practice and other suitable measures are not available. Perhaps the 64 Naming test is less clinically utilised as it belongs to a larger battery of tests and has yet to make the transition into clinical practice.

6.1. Reflection on working with epilepsy and personal impact

This piece of research has provided me with many unique learning opportunities. The most significant of these has been learning about a condition that holds an enormous amount of stigma, even in the 21st century. Reflecting on my clinical experience in epilepsy services, patients are not referred for stigma and coping with epilepsy, but for treatment assessment i.e. surgery. My research led me to reflect upon the reasons why stigma may still surround epilepsy. One possibility is that society responds with fear to what may be perceived as loss of control.

6.2. Self-reflection and conclusions

On reflection I have struggled somewhat to meet the challenges of completing time limited research. I have always had an organised proactive approach towards my work, however due to the change in thesis topic I found it difficult to re-gain my momentum. My ability to cope was also reduced by the fact that I was no longer part of my cohort, who provided a vital support system during training. I acknowledge the value of having supervisors to guide you when completing research. The clinical psychologist's role is one of scientist practitioner, which requires a host of attributes including dedication, motivation and resources. My thesis has allowed me to consider whether a balance between research and clinical practice would be possible, which is something I would endeavour to achieve once qualified. As a result of my learning throughout this thesis, my interest in epilepsy has continued to grow, and I am fortunate to work with this client group clinically. I feel motivated to further consider measures with ecological and cultural validity within this population, and ways in which to improve my clinical practice and develop the service within which I am employed.

References

Bhandari, M., Joensson, A. (2009). *Clinical Research for Surgeons*. Germany: Thieme Publishing Group.

Bozeat, S., Lambon Ralph, M.A., Patterson, K., Garrard, P., & Hodges, J.R. (2000) Non-verbal semantic impairment in semantic dementia. *Neuropsychologia*. 38, 1207–1215.

Clark-Carter, D.C.C. (2010). *Quantitative psychological research, the complete student's companion* (3rd ed.). New York. Psychology press.

Gordis, L. (2004) Epidemiology. Amsterdam: Elsevier Inc.

Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Jacoby, A., Baker, G., Smith, D., Dewey, M., & Chadwick, D.(1993). Measuring the impact of epilepsy: the development of a novel scale. *Epilepsy Research.* 1, 83-8.

Kaplan Goodglass,H.,& Weintraub, S. (1983). *Boston Naming Test.* Philadelphia: Lea & Febiger.

Kosslyn, S.M., & Shin, L.M. (1992). The status of cognitive neuroscience. *Current Opinion in Neruobiology* . 2, p.146-149.

Lambon Ralph,M.A., Ehsan, S., Baker, G.A. & Rogers, T.T. (2012). Semantic memory is impaired in patients with unilateral anterior temporal lobe resection for temporal lobe epilepsy. *Brain*. 135, 242-258.

The human and economic cost of epilepsy in England (2007) – provided by *the All Party Parliamentary Group on Epilepsy*.

Warrington, E.K. (1997) The graded naming test: a restandardisation. *Neuropsychological Rehabilitation*. 7, 143–146.

Keele University

Peer Reviewer's Proforma 03-12-2010

Appendix 3a: Peer review approval

Sheeba Ehsan

Trainee Clinical Psychologist, Clinical Psychology Training Programme Staffordshire University

1st Floor, Mellor Building College Road, Stoke on Trent

ST4 2DF

Dear Sheeba

Illness related knowledge amongst bipolar affective disorder (BAD) patients; validation of an assessment tool

The above project has received final approval from the Independent Peer Review Committee and is permitted to progress for ethical review. Please find attached the peer review comments and accompanying letter for the above project. LREC requests that all peer review proforma/s are sent along with your LREC application form.

Although this project has been deemed appropriate based on scientific merit, you may wish to incorporate the reviewer's constructive comments to strengthen your protocol.

Management approval

You should arrange for all relevant NHS care organisations to be notified that the research will be taking place, and provide a copy of the REC application, the protocol and this letter.

All researchers and research collaborators who will be participating in the research must obtain management approval from the relevant care organisation before commencing any research procedures. Where a substantive contract is not held with the care organisation, it may be necessary for an honorary contract to be issued before approval for the research can be given.

Clinical trial of a medicinal product

Please remember that, if your project is a clinical trial of a medicinal product, MHRA approval is required. You must submit a request for a clinical trial authorisation under the Medicines for Human Use (Clinical Trials) Regulations 2004. Further details can be found at

http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con2022633.pdf

If you have any queries, please do not hesitate to contact Nicola Leighton on 01782

733306. Yours sincerely

Professor Shaughn O'Brien
Chair – Independent Peer Review

Committee CC R&D Office,

Combined Healthcare

Chair

NHS Research Ethics Committee

Dear Sir/Madam

Investigator : **Sheeba Ehsan**

Name of study : **Illness related knowledge amongst bipolar affective disorder (BAD) patients; validation of an assessment tool**

Please find attached the peer review of the above project.

The project was initially awarded a grade 2 (minor revisions were required. Clarification and more information was requested regarding:-

1. Why the impact of psycho-education on care-givers was not considered?
2. Why are measures of self-efficacy not included?
3. Analysis for phase 1
4. And a copy of BAD was requested

The Independent Peer Review Committee are satisfied that the issues raised have been answered and that the project can now be awarded a grade 1 and therefore can proceed for ethical review without any revision.

We have informed the applicant that although this project has been deemed appropriate based on scientific merit, they wish to incorporate the reviewer's constructive comments to strengthen their protocol.
We have also stressed to the applicant that the Independent Peer Review Committee is NOT linked to or a Sub-Committee of the Local Research Ethics Committee and that you may identify ethical issues of your own.

Yours sincerely

Professor Shaughn O'Brien
Chair - Independent Peer Review Committee

Enc

CC R&D Office Combined Health Care

PEER REVIEWER'S PROFORMA

Research Project Details	
Project title	Illness related knowledge amongst bipolar affective disorder (BAD) patients; validation of an assessment
Name of principal investigator	Sheeba Ehsan
Institution of principal	Student

The important or relevance of the problem to be addressed in relation to either or both of:
5. The particular field of research as a whole BAD causes a lot of psychological distress to service-users and carer givers/family members, and so developing an educational tool with the potential to alleviate some of this distress is an important research area. 6. The value of this research for health or social care Increasing understanding of the condition amongst service-users and family member/care- givers will provide a stronger therapeutic environment where service-users are more compliant with treatment, and caregivers will have greater understanding of the needs and plight of the service-users.
The quality and relevance of the background information provided
The literature review is thorough, detailed, knowledgeable, relevant and well written. The context for the proposed study is set by description of a pilot (incidentally, conducted by the supervisor) where validity of the *Bipolar Affective Disorder Interview* [BADI] was assessed in 1 assistant psychologist and 3 service-users.

The design and methods are appropriate to the aim of evaluating the clinical utility of the *Bipolar Affective Disorder Interview* [BADI].

The study is divided into 2 phases:
Phase 1 - content validity of the assessment tool performed using an expert panel consisting of 5 experts, phase 2 - administration of the BADI to 34 service-users pre and post an educational package.

Analysis
Phase 1 - qualitative feedback and
ratings. Phase 2 - repeated measures
t-test

However, I have a number of queries which I'm sure the applicant can easily address.

It appears that the impact of psychoeducation on carer-givers is not being assessed. Please explain why.

Other measures of self-efficacy etc are not included. Please explain

why. A copy of BADI was not included in paperwork. Please

provide.

Details of specifics of analyses for phase 1 qualitative feedback and ratings omitted. Please specify.

If the research presents ethical concerns, does the plan of investigation/scientific background address these concerns?

NB - The final decision about ethics rests with the Local Research Ethics Committee

Main ethical issue is the blurring of boundary between research and clinical care. Letter of invitation for example, doesn't make explicit that the service-user is being invited to participate in a research project.

The quality of analysis provided (statistical or qualitative, as appropriate)

Good as far as it goes. More detail required (see earlier section detailing strengths/limitations.

The capacity and expertise of the research team in the context of the proposed study

Appropriate

Appropriateness of resource requirements

Seems fine

General feedback (indicate major areas where changes will be required, indicate whether any weaknesses indicated in any of the above categories are major or minor areas of concern)

Assessment of Merit		
Grading	**Description**	**Please tick**
1	Proceed without any revision. Project may be submitted for appropriate NHS/University approval and then to either the Local or the Multi-Centre Research Ethics Committee.	
2	Minor amendments or Further information required. Revise project according to reviewer(s) recommendations. Document to be checked by Internal Committee Member prior to Chairman's approval to proceed.	X
3	Complete major revision required. Principal Investigator to discuss outcome with Centre/Programme Director and agree plan to complete substantive revision of the project (with support as agreed). Resubmission will need to be reviewed and approved by Internal Committee Member, prior to Chairman's approval to proceed.	
4	Reject on the basis that the project has major scientific flaws	

Please e-mail completed form to Nicola Leighton, Research Governance Administrator (n.leighton@uso.keele.ac.uk) with a paper copy being sent with your signature.