MEMORY IN CHILDREN WITH TEMPORAL AND FRONTAL LOBE EPILEPSY, PRE- AND POST-OPERATIVELY

A Doctoral Dissertation

Presented to

The Faculty of the Department

Of Psychology

University of Houston

In Partial Fulfillment

Of the Requirements for the Degree of

Doctor of Philosophy

By

Rebecca B. Martin

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Abstract

Temporal lobe epilepsy (TLE) has been shown to be related to cognitive impairments in adults and children. This study specifically focuses on the cognitive impairments that can be associated with surgical intervention for intractable epilepsy in children. In adults, there is evidence for material-specific memory decline such that those with L-TLE have impaired verbal memory while those with R-TLE tend to have impaired visual memory, though the latter results are less robust. In children, the results are mixed suggesting that both verbal and visual memory can be affected by L- or R-sided TLE. In the current study, measures of objective memory, including immediate, delayed, and recognition memory, as well as verbal and non-verbal memory, everyday memory, and academic skills were considered pre- and post-surgery in children with TLE as well as in comparison groups of children with surgical intervention for frontal lobe epilepsy (FLE), for parietal or occipital lobe epilepsy, and children who have not had surgery. The impact of seizure-related variables, including seizure frequency, change in medications, age at surgery, age of onset of seizures, follow-up interval, and involvement of the hippocampus was explored. Results showed that the Surgery and No Surgery groups differed on academics: children without surgery declined but the surgery group were unchanged. The combined TLE and FLE group performed worse than children with parietal or occipital surgery on measures of objective memory, though neither group changed significantly. The combined TLE groups declined on immediate and delayed memory while the FLE improved. Finally, this study was consistent with the current literature for lack of evidence to support material-specific decline or improvement after surgery in the L- and R-TLE groups. Only the different etiologies (MTS, tumor, cortical dysplasia, etc.) may have impacted performance in the TLE group. While there was evidence for decline in immediate and delayed memory for the TLE groups, this does not appear to affect everyday memory or academic functioning.

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Memory in Children with Temporal and Frontal Lobe Epilepsy, Pre- and Post-Operatively

Epilepsy is the third most common neurological condition in adults (Epilepsy Foundation) and the most common in children (Hauser & Hesdorffer, 1990). It is a condition characterized by recurrent seizures (at least two) that are the result of abnormal electrical activity in the brain. An individual must have at least two unprovoked seizures to be diagnosed with epilepsy. Seizures are typically classified according to the origin of the electric discharge. Partial seizures begin in a focal brain region and may be preceded by an aura, or warning sign. Partial seizures can be simple, with no loss of consciousness or memory for the event, or complex, with an alteration of consciousness. The most common origin of complex partial seizures is the temporal lobe, followed by the frontal lobe (Hannay, Howieson, Loring, Fischer, & Lezak, 2004). Additionally, if the seizure activity spreads in the brain, an individual may experience a secondary generalized seizure, which entails sudden, synchronous bilateral epileptic discharges that typically result in a loss of consciousness.

Seizures are typically treated with anti-epileptic medications. However, when seizure freedom or significant reduction cannot be achieved, surgical intervention is considered. The impact that this type of surgery can have on cognitive functioning is important to understand because it contributes to the balance between the negative impact of the seizure disorder with the negative consequences of the surgery. Therefore, the goal of the current study is to address how such surgery impacts cognitive processes, with a focus on memory in children.

Cognitive Effects of Epilepsy in Adults and Children

Epilepsy syndromes have been associated with a wide range of cognitive problems including decreased overall intelligence, memory, and executive functions. Cognitive dysfunction may arise from: (a) the disruption caused by the seizure event themselves (Dickson et al., 2006); (b) the iatrogenic effects from the antiepileptic drugs (AEDs) used to treat seizures; or (c) the underlying neuropathology that produces the seizures (e.g. brain tumor; Helmstaedter & Kockelmann, 2006). Much of what is known about the effects of epilepsy on cognition comes from adults with temporal lobe epilepsy (TLE). In children, research is emerging on the effects of TLE on cognition. For both adults and children however, much of the data is focused on general cognitive functions (such as IQ) rather than more specific cognitive functions (including memory). Further, cognitive function in epilepsy may be influenced by the seizure disorder itself, as well as by the surgery used to treat severe seizure disorders. A comparison between children who do and do not get surgery is complicated because surgery is typically undertaken only when the seizure disorder is severe and when a single focus has been identified. Therefore below, the current literature of IQ and memory function in these groups without surgical intervention is reviewed followed by the research on pre- and post-surgical performance.

IQ. There is some evidence of general cognitive impairment (lower IQ) in adults with TLE (Black, Schefft, Howe, Szaflarski, Yeh, & Privitera, 2010; Oyegbile, et al., 2004; Wang et al., 2012); for example, Helmstaedter and Kockelmann (2006) found that 30% of their patients with TLE had an IQ below 85 compared to about 16% of the general population. Decline in IQ scores over time in TLE is less clear. Intelligence scores may decline over time in TLE; however, this may be related to seizure frequency (Dodrill, 2004). Even so, some research has shown no decline in IQ in TLE even when status epilepticus was considered (Adachi et al., 2005). In a cross-sectional study examining IQ across the lifespan in patients with TLE, Baxendale and colleagues (2010) found that IQ was unchanged until at least age 60, despite continued seizures. When seizures are well controlled, intelligence scores may even improve over time (Dodrill & Wilensky, 1990; Rodin, 1968; Seidenberg, O'Leary, Berent, & Boll, 1981; Selwa, Berent, Giordani, Henry, Buchtel, & Ross, 1994). Therefore, while there is evidence for decreased IQ in adults with TLE relative to controls, literature is mixed regarding a decline in overall IQ over time in adults with TLE, which could suggest variability in the specific cognitive functions that are affected vs. unaffected.

There are fewer pediatric studies on the association of epilepsy and IQ, relative to the adult literature. Studies have shown that there is a wide range of intellectual performance that can be attributed to the heterogeneity of epilepsy disorders. For example, children with TLE have been found to have intelligence scores in the mildly impaired range (Nolan et al., 2003) to the lower end of the average range (Lah, 2004). Further, children with generalized symptomatic epilepsy (i.e. usually with a known neurological cause) and non-localized partial epilepsy had IQ scores in the moderately to severely impaired range, while children with generalized idiopathic epilepsy (i.e. with no known cause) and children with seizure foci outside of the temporal or frontal lobes, had IQ scores in the low average to average range (Nolan et al., 2003). For change over time, prospective studies have shown generally unchanged IQ over time for most children with TLE (Bourgeois et al., 1983; Ellenberg, Hirz, & Nelson, 1986). However, it has been proposed that general intellectual functioning can decrease over time if the seizures are not well controlled (Dodrill, 2004). Children with TLE whose IQ did decline over time had a more severe seizure disorder (greater frequency of seizures), an earlier onset, and a greater incidence of drugs in the toxic range (Bjornaes, Stabell, Henricksen, & Loyning, 2001; Bourgeois et al., 1983). In addition to TLE, research that examined intellectual functioning in children with Frontal Lobe Epilepsy (FLE; Nolan et al, 2003; Hernandez et al., 2001; Mateer & Williams, 1991) found average intellectual performance. The preponderance of the literature has shown mildly impaired IQ in children with TLE and average intelligence in children with FLE and has supported an unchanged IQ over time in children with epilepsy, although seizure factors such as frequency and age at onset may be related to the stability of general cognitive outcomes in children.

Memory. In adults, approximately 70% of patients with TLE experience memory difficulties, making it the most common specific cognitive finding in this population (Helmstaedter & Kockelmann, 2006). Specifically, impairments are seen in learning and storing new semantic material, which are functions known to be supported by areas of the temporal lobe, including the hippocampus. These memory impairments appear to be material specific, with impairments in verbal memory typically seen in adults with left or dominant hemisphere TLE (Frisk & Milner, 1990; Helmstaedter & Kockelmann, 2006; Scoville & Milner, 1957). A systematic review found that verbal memory decline following left-sided temporal surgery is twice as high as the rate of non-verbal memory decline in patients with right-sided temporal surgery (Sherman et al., 2011). Further, research in adults with left TLE (L-TLE) has found a link between temporolateral structures and verbal short-term memory, while temporomesial structures are associated with verbal long-term consolidation and retrieval processes (Helmstaedter, Grunwald, Lehnertz, Gleibner, and Elger, 1997). Verbal recognition is associated with the anterior temporal lobe (Helmstaedter, Grunwald, Lehnertz, Gleibner, and Elger, 1997). Other research has shown no relation between the hippocampus and recognition memory (Aggleton & Shaw, 1996; Aggleton & Brown, 1999; Baxendale, 1997; Hendriks, Kampen, Aldenkamp, van der Vlugt, Alpherts, & Vermeulen, 2003; Hermann et al., 1995). Non-verbal immediate and delayed memory may be associated with right or non-dominant hemisphere TLE, although the association is less robust than between verbal memory and L-TLE (Barr, 1997; Baxendale, Thompson, & Van Paesschen, 1998; Feigenbaum, Polkey, & Morris, 1996). Definitive findings regarding the non-verbal/right hemisphere association is complicated by the difficulty in developing truly non-verbal tests that do not involve covert verbal strategies (Wang et al., 2011) and by greater heterogeneity in the measures used relative to verbal memory (Lee, Yip, & Jones-Gotman, 2002).

For children, two studies showed memory differences between patients with L-TLE and R-TLE; individuals with L-TLE performed more poorly on tasks of verbal memory, whereas those with R-TLE perform more poorly on tasks of non-verbal memory (Fedio & Mirsky, 1969; Jambaque, Dellatolas, Dulac, Ponsot, & Signoret, 1993). Such findings are consistent with the adult literature. Fedio and Mirsky (1969) found decreased immediate and delayed verbal memory in the L-TLE group and decreased delayed non-verbal memory in the R-TLE group. Jambaque and colleagues (1993) found that their L-TLE group performed worse on delayed relative to immediate verbal memory. Another study (Cohen, 1992) found that performances on verbal and non-verbal memory did not significantly differ between the R-TLE and L-TLE groups, but there were trends in the expected directions (i.e., R-TLE performed worse on non-verbal memory than the L-TLE and vice versa). Further, the L-TLE group performed significantly worse than the control group on verbal memory tests while the R-TLE group did not differ significantly from the controls. Still other studies have found decreased verbal and non-verbal memory compared to controls, regardless of seizure laterality (Camfield et al., 1984; Kernan et al., 2012). It has been suggested that the lack of clear material specific differences for children may be due to less lateralized brain organization in childhood or possibly reorganization in brain function (Williams & Sharp, 1998).

Additionally, some research on children with FLE has found deficits in verbal and non-verbal memory similar to those found in TLE (Hernandez et al., 2003; Jambaque et al., 1993; Kemper, Helmstaedter, Holinka, & Elger, 1992, as cited in Hernandez et al., 2003). Such deficits may be related to executive dysfunction, as children with FLE make more errors of perseveration, repetition, intrusions, and source memory (Hernandez et al., 2003), and the tasks showing impaired performance require planning and organization strategies that are also related to the frontal lobes (Jambaque et al., 1993). However, other research has found memory performance in FLE to be in the average range and higher than TLE memory performance (Culhane-Shelburne, Chapieski, Hiscock, & Glaze, 2002; Delaney, Rosen, Mattsen, & Novelly, 1980).

In summary, research with adults suggests that individuals with L-TLE are at risk for verbal memory impairments, with a less clear association of R-TLE and non-verbal memory. In children, while there is some evidence for lateralized differences in specific memory deficits, the majority of the research supports a more mixed profile, sometimes with decreased verbal and non-verbal memory overall and difficulties in both immediate and delayed memory have been observed. Children with FLE may also have deficits in aspects of verbal and non-verbal memory (Hernandez et al., 2003), but may do so for different reasons than children with TLE.

Cognitive Effects of Surgical Intervention in Adults and Children with TLE

Temporal lobectomy and related surgical procedures are interventions for seizures that are unresponsive to medication. The prevalence of surgical intervention in children has been estimated to occur in about 10% of newly diagnosed cases of epilepsy in the United States each year (Berg et al., 2009). However, surgery also carries a risk for loss of cognitive function (Helmstaedter & Kockelmann, 2006). A decline in function would be expected with removal of brain tissue that is critical for support of that function. For example, with temporal lobectomy one might expect memory decline; however, the risk for decline would be reduced if damaged brain tissue were not supporting that function prior to surgery. Additionally, reduced seizure burden and anticonvulsant medication would likely improve alertness, attention, and processing speed, and consequently, memory performance.

Adults. The majority of surgical studies have focused on memory changes in adults with temporal lobe seizures. Findings have been generally consistent in demonstrating risk for verbal memory decline following surgery for left (or dominant hemisphere) TLE, with a less consistent overall trend for declines in non-verbal memory after surgery for right (or non-dominant) TLE (Baxendale et al., 1998; Chelune, Naugle, Luders, & Awas, 1991; Gleissner, Helmstaedter, Shramm, & Elger, 2002; Helmstaedter, Richter, Roske, Oltmanss, Shramm, & Lehmann, 2008; Jones-Gotman et al., 1996; Lee, Yip, & Jones-Gotman, 2002; Powell, Polkey, & McMillon, 1985). The aforementioned studies do not assess factors contributing to the decline observed in the L-TLE group, with the exception of the extent of hippocampal involvement, and findings regarding hippocampal involvement have been variable. The pattern of results recapitulates the non-surgical relationships between left and right TLE and verbal and non-verbal memory, as described above. There is some evidence for improvement in verbal memory associated with the resection of the non-dominant lobe, and improvement in non-verbal memory associated with resection of the dominant lobe (Invik, Sharbrough, & Laws, 1987; Saykin et al., 1992). Such findings may be attributable to improvements in alertness and processing speed due to seizure control and anticonvulsant medication reduction.

Children. Studies that included children and that conducted pre- and post-surgical assessments of memory were systematically reviewed (24 in total). The focus was on the studies that are most informative about the risk for decline in memory functions associated with pediatric TLE surgery. Studies were excluded for a number of reasons, including combined adult and pediatric populations (Cavazutti, Winston, Baker, & Welch, 1980; Dennis, Farrell, Hoffman, Hendrick, Becjer, & Murphy, 1988; Mizrahi, et al., 1990; Robinson et al., 2000), used adult memory tests (Adams, Beardsworth, Oxbury, Oxbury, & Fenwick, 1990; Lewis, et al., 1996; Meyer, Marsh, Laws, & Sharbrough, 1986), or had IQ as the only outcome measure (Korkman et al., 2005). The remaining 16 studies are summarized in Table 1 and are reviewed below. Given the rarity of the population studied and the specific focus of research, it is perhaps not surprising that significant methodological limitations are frequent even in this restricted sample of the literature. Therefore other research studies were retained despite some significant limitations such as patients included patients with an IQ of less than 70 (Chieffo et al., 2011; Dlugos, Moss, Duhaime, & Brooks-Kayal, 1999; Hepworth & Smith, 2002; Lah et al., 2002), or had a sample size of less than 10 per group (Szabo, et al., 1998; Williams, Griebel, Sharp & Boop, 1998).

Many studies of pre-post surgery in children with TLE reported either no change in memory function from pre- to post-assessment (Chieffo et al., 2010; Kuehn et al., 2002; Lendt, Helmstaedter, & Elger, 1999), or improvements in function (Beardsworth & Zaidel, 1994; Gleissner et al., 2002; Gonzalez, Mahdavi, Anderson, & Harvey, 2012; Jambaque et al., 2007; Mabbott & Smith, 2003). Specifically, improvements were found in immediate and delayed facial recognition tasks (Beardsworth & Zaidel, 1994; Gonzalez et al., 2012; Mabbott & Smith, 2003), rote immediate verbal memory (Gleissner et al., 2002), and an overall composite of verbal memory scores (Jambaque et al., 2007). Interestingly, studies that reported significant decline in memory following surgery involved very small sample sizes (Dlugos et al., 1999; Szabo, et al., 1998; William et al., 1998). Szabo and colleagues found that immediate verbal memory declined in those who had higher scores at baseline and those who had left versus right sided epilepsy foci, whereas delayed verbal memory declined significantly regardless of baseline performance or laterality. In contrast, the Williams et al. study found only a decline in delayed, rather than immediate, verbal memory. The difference between immediate and delayed verbal memory was not reported in the Dlugos et al. study; however, four of their eight patients showed a decline in overall verbal memory. None of these three studies showed the significant lateralized, material-specific declines that have been reported with adults. Another study showed decreased delayed visual memory in the TLE group while visual memory for the FLE group was unchanged; laterality was not assessed and only a composite of immediate and delayed verbal memory was considered (Chieffo et al., 2010). Another study included children with TLE, but did not specifically examine group differences; however, using standardized regression-based analysis of change scores, they found that the children in their study who declined on the Verbal Memory Index (from the Test of Memory and Learning, second edition; which includes only immediate memory) were those with left TLE (Meekes, Braams, Braun, Jennekens-Schinkel, van Nieuwenhuizen, on behalf of the Dutch Collaborative Epilepsy Surgery Programme, 2013). Although there was evidence of improvement in immediate verbal memory in the Gleissner et al. (2002) study, this recovery was not seen in delayed verbal memory for the L-TLE group and the L-TLE group did not differ significantly from the R-TLE group on post-test. There was only one study that found laterality differences in change scores on immediate and delayed facial recognition tasks (Beardsworth & Zaidel, 1994) – children with right temporal lobectomies improved while those with left temporal lobectomies did not change. Verbal memory was not assessed in that study.

When the informative studies of children with TLE pre- to post-surgical assessments are considered across the cognitive areas most commonly examined, the majority of the research shows that for children who undergo right or left temporal lobectomies, memory performance is unchanged pre-post surgery, or else memory performance is improved. Nonetheless, some research has found evidence of decline in immediate and delayed verbal memory. There is little evidence to suggest that laterality of seizure focus (and therefore of surgical intervention) influences whether a child will improve, be unchanged, or decline following surgery. However, laterality relationships are seen in the adult literature, studies that tend to involve larger samples, and therefore it is possible this relationship also exists within pediatric populations. Therefore, at this time the literature does not provide a consensus regarding the impact of surgical intervention on memory in left and right TLE. This area of research would benefit from more studies with multiple comparison groups, inclusion of both pre- and post-assessment data, and comparison of immediate, delayed, and recognition memory in order to help provide clarity to surgical effects.

Surgical Intervention in FLE

Surgery for frontal lobe epilepsy (FLE) accounts for 6 – 30% of epilepsy surgeries in adults, second only to temporal lobe surgeries (Hosking, 2003; Janszky et al., 2000). However, a common neuropsychological profile of adult patients who have undergone surgery for FLE has not yet been established. This may be due in part to the diffuse nature of frontal lobe seizures or the wide range of functions associated with the frontal lobe and the lack of tests adequate to detect these subtleties (Risse, 2006; Stuss, 2011). While Risse et al. (1996) reported that word fluency declined following left frontal lobe surgery and design fluency declined following right frontal lobe surgery, these authors suggested that size and region of the resection may actually have been more related to the outcomes than hemisphere (Risse, 2006). Other research with patients with frontal lobe lesions has shown that recognition memory is also impaired, more so than recall (Baldo, Delis, Kramer, & Shimamura, 2001). Further, patients with frontal lobe epilepsy made more false positive errors than patients with temporal lobe epilepsy on recognition paradigms (Swick & Knight, 1999).

For pediatric studies, concerns similar to those of adults exist (nature of the frontal lobe as well as lack of adequate measures), but there is also the added consideration of the development of the frontal lobes through adolescence, suggesting that the observed profile will be highly dependent on age of surgery (Lendt et al., 2002). While research on children with FLE shows they too may be at risk for decreased memory performance, there are very few studies of pre- to post-surgery cognitive change in children who have undergone surgery for FLE. Two studies were identified, both of which compared a FLE group to a TLE group. Lendt et al. (2002) showed pre- to post-surgery improvements for the FLE group in attention, processing speed, working memory, and fine motor skills, as well as on measures of verbal and non-verbal recognition memory. However, a second study found declines in aspects of executive function, such as verbal fluency and problem solving, while memory performance were unchanged in the FLE group (Chieffo et al., 2011). Neither study compared groups on immediate, delayed, and recognition memory, although differential performance in these types of memory recall have been demonstrated in TLE. Although these two studies did not show memory difficulties in children with FLE, if such difficulties do occur they may differ from those of TLE because frontal lesions impact memory differently than lesions of the mesial temporal lobes (Baldo & Shimamura, 2002), and that difference may translate into more difficulties with everyday memory for the FLE group relative to the TLE group. By including FLE as a comparison group, the present study has the potential to characterize more specifically the memory pattern in these groups relative to one another.

Functional Outcomes

Very little is known about whether changes in test performance after surgery are noticed in a patient’s day-to-day activities, which for children include everyday memory and learning as well as academic performance. Whether declines or improvements in performance on tests of memory are reflected in patients' memory and learning in their everyday life is unclear. Studies of adult patients have found little or no relationship between the patients' subjective reports and their performance on tests of memory, although patient reports have been correlated with mood (Giovagnoli, Mascheroni, & Avanzini, 1997). There have been few studies to address this question in the pediatric population and the findings have been inconsistent. Gonzalez et al. (2008) found a significant correlation between test performance and parental report of everyday memory in a group of young patients with TLE, while Kadis and colleagues (2004) failed to find a significant relationship. Both studies involved small samples that included children with significant intellectual impairment. Chapieski, Evankovich, Hiscock, and Collins (2011) studied a larger group of children with epilepsy and without significant verbal impairments. They did not find a significant relationship between parental report and test performance but did find a limited relationship between the child's report of everyday memory and performance on a test of memory. The results of Chapieski and colleagues also suggested that, similar to the adult studies, reports of everyday memory in this group of children are impacted by mood and attention.

There are few studies of the relationship between pre- to post-surgical changes in memory test performance and reports of everyday memory. One study with adults (Sawrie et al., 1999) and one with a pediatric group (Smith, Elliott, & Lach, 2006) were identified. Neither found that changes in memory test performance were related to subjective assessments of everyday memory. The study by Smith and colleagues, however, relied on reports of memory complaints from medical records rather than a more formalized assessment of everyday memory.

A review by Reilly and Neville (2011) on the prevalence of low academic achievement in epilepsy found that most children who do not have intellectual disability perform in the average range on teacher ratings of academic achievement and on standardized testing. Children with idiopathic and cryptogenic epilepsies however have been shown to be at greater risk for repeating a grade and/or for requiring more academic assistance than other children (Oostrom, Smeets-Schouten, Kruitwagen, Peters, & Jennekens-Schinkel, 2003). Additionally, several studies have reported that children with epilepsy exhibit decreased performance in at least one academic area (Fastenau, Shen, Dunn, & Austin, 2008; Mitchell, Chavez, Lee, & Guzman, 1991; Piccinelli et al., 2008; Shoenfeld et al., 1999; Tedrus, Fonseca, Melo, & Ximenes, 2009).

Only one study has compared academic achievement before and after surgery for intractable epilepsy in children. In that study, Williams and colleagues (1998) found that academic skills, including word reading and spelling, were generally in the average range prior to surgery, with only math skills in the low average range. There were no significant changes following surgery. However, children in this study were not compared by epilepsy classification and therefore, it is unknown whether children with FLE and TLE differ in their academic performance measures. Given the limited current knowledge, further assessment of the impact of surgical intervention on academic performance is warranted.

Seizure-related Variables

Seizure-related variables, such as age of onset, frequency of seizures, duration of seizure disorder, follow-up interval, origin of seizures, and etiology of epilepsy, can affect cognition with or without surgical intervention. For adults, seizure frequency (Wachi et al., 2001), early seizure onset (Glosser et al., 1997), and either higher doses or polytherapy with antiepileptic drugs (AEDs; Kwan & Brodie, 2001) are associated with lower levels of cognition. Several pediatric studies have noted that duration of epilepsy disorder is negatively related to cognitive outcomes (Gleissner et al., 2002; Mabbott & Smith, 2003; Westerveld et al., 2000), though reporting of other seizure-related factors is variable across pediatric studies.

Hepworth and Smith (2002) found that patients with right temporal resection performed worse than those with left resection on measures of verbal and non-verbal memory, a result the authors attributed to the fact that children who had right-sided resections took more medications and were less likely to be seizure free following surgery relative to those with left-sided resections. Similarly, Lendt and colleagues (2002) found that being seizure free post-surgery was related to an increase in short term memory (measured with a composite of digit and spatial spans as well as digit span backwards), although some improvements in attention as well as verbal and non-verbal memory were noted even among those who continued to have seizures. Such results are consistent with other research that has found seizure freedom was related to improved behavior and attention (Gleissner et al., 2008), as well as unchanged or improved memory (Lendt et al., 1999). Further, Kernan et al. (2012) found that higher seizure frequency in a group of children with complex partial epilepsy was associated with poorer performance on measures of immediate and delayed verbal memory. However, these studies did not assess the change in seizure-related variables from pre- to post-surgery. Using standardized regression-based scores, Meekes et al. (2013) showed that those who continued to take medications two years after surgery had lower scores than those without medications. However, this study did not measure differences by location of surgical intervention.

Children with surgery at older ages tend to have worse outcomes (Jambaque et al., 2007; Westerveld et al., 2000). Studies that have assessed children at shorter follow-up periods (<6 months post-surgery) have also been more likely to find declines in memory (Gleissner et al., 2002; Kuehn et al., 2002; Szabo et al., 1998). Gleissner et al. (2005) reported declines in verbal memory in children and adults three months after surgery, that recovered by twelve months for children but not for adults. Gleissner et al. (2002) also found that follow-up memory performance were worse in children where the hippocampus was removed during surgical intervention.

Findings for seizure-related variables have been inconsistent, and therefore firm conclusions are difficult to make about their association to cognitive performance. However, the evidence does suggest that it would be relevant to examine variables such as change in number of medications, change in seizure frequency, whether the hippocampus was part of the surgical resection, age of seizure onset and duration, and age at surgery.

Present Study

The goal of the proposed study is to help clarify the functional risks and benefits of surgery for pediatric patients with intractable seizures. As the literature suggests, surgical intervention appears to lead to better overall cognitive functioning compared to those who do not have surgery. The current study will further elucidate the impact of surgery by including multiple comparison groups and considering the impact of seizure-related variables on the outcomes. Current research has primarily focused on performance on clinical tests of memory, although further studies are still needed. Little is known about the impact of surgery on everyday functioning. The present study will assess not only objective memory, but also everyday memory and academic skills.

Participants included children with the most common seizure foci requiring surgical intervention (L-TLE, R-TLE; FLE). These groups were contrasted with two others: those whose surgery involved resections in either the parietal or occipital lobes (sites that presumably carry less risk for memory impairment), and those with intractable seizures who did not receive surgery but were evaluated on two occasions. The focus of the current study was on children who were assessed at least one year after surgery (or after initial assessment), in an attempt to reflect more stabilized cognitive functions. Finally, the study evaluated the contribution of seizure-related variables to all outcomes. These include age of onset, age at surgery, change in seizure control, change in the number of anticonvulsant medications, length of follow-up interval, and whether the hippocampus was resected (for TLE only).

Hypotheses

The following research questions and hypotheses were addressed:

Question 1. Does surgery per se result in improved aspects of cognition? Individuals in the four surgery groups (R-TLE, L-TLE, FLE, and Other) were combined, and then compared to the non-surgery group on composite measures of objective memory, everyday memory, and academic achievement.

Hypothesis 1a: The combined surgery group will demonstrate a greater increase over time in objective memory test performance relative to the non-surgery group.

Hypothesis 1b: The combined surgery group will demonstrate a greater increase over time in everyday memory relative to the non-surgery group.

Hypothesis 1c: The combined surgery group will demonstrate greater increase over time on measures of academic skill relative to the non-surgery group.

Question 2. While it may be expected that surgical intervention will result in improved or unchanged overall cognitive functioning compared to no surgery, is there risk for decline in specific areas of function that are dependent on particular regions of the brain affected by the seizure disorder? For example, do temporal and frontal lobe resections pose more risk for decline in objective memory than resections outside of these brain areas? The primary contrast for this hypothesis was between a combined FLE and TLE group versus the Other seizure group. The dependent variables were the same as those examined in Hypothesis 1.

Hypothesis 2a. Due to the association of the frontal and temporal lobes with aspects of memory, declines in performance on a composite score of objective memory will be greater for the TLE and FLE surgery groups combined, relative to the Other surgery group.

Hypothesis 2b. Declines in performance on the total score for the everyday memory tests will be greater for the combined TLE and FLE surgery group than for Other surgery group.

Hypothesis 2c. Given the role of memory on other functions, including learning, declines in performance on a composite score of the academic achievement tests will be greater for the combined TLE and FLE surgery group than for the Other surgery group.

Question 3. Do temporal lobe resections pose more of a risk for functional decline than frontal lobe resections? The primary contrast for this hypothesis was between the combined TLE group versus the FLE group.

Hypothesis 3a. Declines in performance on immediate recall of verbal and non-verbal memory will be greater for the combined TLE group than for the FLE group.

Hypothesis 3b. Declines in the performance on delayed recall memory tests will be greater for the combined TLE group than for the FLE group.

Hypothesis 3c. Declines in the performance on recognition memory tests will be greater for the FLE group than the combined TLE group.

Hypothesis 3d. Declines in everyday memory will be greater for the FLE group than the combined TLE group.

Hypothesis 3e. Will the combined TLE versus FLE groups differ on measures of academic skills?

Question 4. Given the expected results of Hypotheses 1, 2, and 3, is there evidence of lateralized, material specific changes in the temporal lobe group? Thus, the primary contrast for this hypotheses is between the groups of children with R-TLE versus those with L-TLE.

Hypothesis 4a. Improvements in performance on immediate recall verbal memory tests will be greater for the R-TLE group than the L-TLE group.

Hypothesis 4b. Improvements in performance on immediate recall non-verbal memory tests will be greater for the L-TLE group than the R-TLE group.

Hypothesis 4c. Improvements in performance on delayed recall verbal memory tests will be greater for the R-TLE group than the L-TLE group.

Hypothesis 4d. Improvements in performance on delayed recall non-verbal memory tests will be greater for the L-TLE group than the R-TLE group.

Question 5. Are any of the functional changes predicted in Hypotheses 1, 2, 3, and 4 related to changes in seizure control, changes in number of medications, follow-up interval, age of onset, or age at surgery?

Methods

Participants

Children who received baseline neuropsychological testing as part of an evaluation for surgical intervention for intractable epilepsy at Texas Children's Hospital and whose parents consented to be included in future research were entered into a database and considered for this study (*N*=113). Children were excluded from entry into the database if the Full Scale IQ was below 60; the number of these children who may have been excluded is unknown. Children were also excluded if they underwent a hemispherectomy (*n* = 3) or callosotomy (*n* = 1), seizure origin was global, unclear (*n* = 2), or included both the frontal and temporal lobes (*n* = 2), or were older than 18 or younger than 6 at baseline (*n* = 2). Therefore, the initial baseline sample consisted of 103 eligible children. Of these 103, 55 children returned for a second follow-up evaluation, and were compared with the 48 children who did not return for a second visit on the demographic variables used in this study. Table 2 displays descriptive data for these two groups, as well as for the sample as a whole. It should be noted that seizure frequency was assessed as total seizures over the previous three months and the age of onset is reported in years. Returning children and non-returning children did not differ on any of the demographic or seizure-related variables. One individual (with FLE) who had two time points had very limited cognitive data at baseline, and so was excluded from all remaining analyses. Table 2 also presents descriptive data for cognitive variables, where 102 children are represented (54 children who had two visits to 48 children with only a baseline visit); these individuals were used to standardize the composite variable used in analyses (explained in detail below). These two groups did not differ on any of the cognitive measures used in this study.

The final analyzable sample consisted of 54 children organized into one of five groups. Across groups, the average age at baseline testing was 13.5 years (SD = 2.7), the average age of seizure onset was 7.0 years (SD = 4.1), the mean receptive language score on the PPVT was 93.0 (SD = 13.8), the mean Verbal IQ was 91.4 (SD = 11.9), and mean Non-verbal IQ was 97.5 (SD = 12.1). Four of these groups received surgery: right temporal lobe (R-TLE, *n* = 11), left temporal lobe (L-TLE, *n* = 15), frontal lobe (FLE, *n* = 10), and parietal or occipital group (Other, *n* = 8). Group designation was determined through review of the neurosurgical report that described the results of scalp EEG and the location of resection. The fifth group was a non-surgical control group with different seizure foci (*n* = 10; 1 R-TLE, 3 L-TLE, 6 FLE). Typically individuals did not undergo surgery because the family decided against it or a specific target area could not be confirmed, although this information was not available for individuals in this group. Etiologies within the L-TLE group were cortical dysplasia (*n* = 4), tumor (*n* = 4), mesial temporal sclerosis (MTS, *n* = 4), hydrocephalus (*n* = 1), MTS plus cortical dysplasia (*n* = 1), and MTS plus tumor (*n* = 1); R-TLE etiologies included cortical dysplasia (*n* = 2), tumor (*n* = 6), MTS (*n* = 1), cortical dysplasia plus gliosis (*n* = 1), and neurocystercicosis (*n* = 1); FLE etiologies included cortical dysplasia (*n* = 7), tumor (*n* = 2), and encephalitis/infection (*n* = 1); Etiologies of the Other subgroup consisted of cortical dysplasia (*n* = 6) and tumor (*n* = 2); and etiologies of the No Surgery consisted of cortical dysplasia (*n* = 5), tumor (*n* = 1), and MTS (*n* = 1). Data is unknown for 3 patients (No Surgery group).

Procedure

Children were referred for a neuropsychological evaluation as part of a routine work-up for epilepsy surgery. Children were seen for a second clinical evaluation approximately 1 year following surgical intervention or 1 year after the baseline evaluation for those who did not undergo surgery; however, the follow up times were variable (range 6 – 63 months; mean = 25 months). Those who did not have a second clinical evaluation were recruited for a research evaluation; all were in the No Surgery group (*n* = 4). A standard neuropsychology battery was administered in two 3-hour sessions over one or two days for the clinical assessments and a reduced 4-hour battery for the research assessments.

Measures

Descriptive Measures. The measures below were included to describe the sample and to screen for language problems. They are not included in any hypotheses.

Intelligence. The *Wechsler Intelligence Scale for Children – 4th edition (WISC-IV*; Wechsler, 2003), *Wechsler Adult Intelligence Scale – 4th Edition (WAIS-IV;* Wechsler, 2008)*,* or the *Wechsler Adult Intelligence Scale – 3rd edition (WAIS-III*; Wechsler, 1997) were used as measures of intelligence, depending on the child's age at baseline assessment. The *Verbal Comprehension Index (VCI)* and the *Perceptual Reasoning Index (PRI)* from the WISC-IV and WAIS-IV and the *Verbal IQ (VIQ)* and *Performance IQ (PIQ)* scores from the WAIS-III were used for exclusion criteria and sample description. The corrected test-retest reliability is $r = .93$ for the WISC-IV VCI, $r = .89$ for the WISC-IV PRI, $r = .96$ for the WAIS-IV VCI, $r = .87$ for the WAIS -IV PRI, $r = .94$ for the WAIS-III VIQ, and $r = .88$ for the WAIS-III PIQ.

Language. The *Peabody Picture Vocabulary Test-4th Edition (PPVT-IV*; Dunn & Dunn, 2007*)* was used to assess for language concerns. This is a screening test of verbal ability and a measure of receptive single-word vocabulary. The child is shown a page with four pictures and the examiner provides the child with a vocabulary word. The child is asked to identify the picture that best describes the word either by pointing or verbalizing the number of the picture. The child continues until 8 of 12 items are missed in an item set. There are two alternate forms (Form A and B) Standard scores were used to describe the sample. The mean internal consistency is $\alpha = .97$ for Form A and $\alpha = .96$ for Form B.

Objective Memory Tests.

Verbal memory. Subtests from the *Wide Range Assessment of Memory and Learning- 2nd edition* (WRAML-2; Sheslow & Adams, 2011) and the *Test of Memory and Learning – 2nd edition* (TOMAL-2; Reynolds & Voress, 2007) were used. In the WRAML-2 *Story Memory subtest,* an individual is asked to listen to and remember two short stories with immediate and delayed (20 minute) recall. The median internal consistency is $\alpha = 0.91$. The WRAML-2 *Verbal Learning (VL)* subtest consists of five trials of a word list with a delayed recall component after 20 minutes. The median internal consistency is $\alpha = 0.91$. The TOMAL-2 *Paired Recall (PR)* is a verbal paired-associate learning task in which the child is asked to recall a list of words pairs when the first word is provided by the examiner. Easy and hard pairs are provided. The median internal consistency is α = .86.

Non-verbal memory. The TOMAL-2 *Facial Memory (FM)* and the *Visual Selective Reminding (VSR)* subtests were used to assess non-verbal memory. FM is a subtest requiring recognition and identification of black-and-white photos of faces from a set of distractors. The faces are those of males and females of various ages and ethnic backgrounds. There is a delayed recall for this task. The median internal consistency for immediate recall is α = .82 and α = .88 for delayed recall. VSR is a non-verbal subtest requiring children to point to specific dots on a card following a demonstration by the examiner. The individual is only reminded of the items recalled incorrectly and trials continue until mastery is achieved or 8 trials have been attempted. There is a delayed recall for this task. The median internal consistency for immediate recall is α = .92 and α = .67 for delayed recall.

Behavioral Questionnaires.

Everyday Memory. The *Everyday Verbal Memory Questionnaire* (EVMQ) was originally developed with a sample of 267 parents and their children who had been diagnosed with a range of neurological disorders. There are 30 items on each of the scales (parent and child versions) that are scored on a 5-point likert scale. An exploratory factor analysis using principal axis factoring with varimax rotation revealed two factors for each version: Prospective Memory (PM) and Learning/Retrieval (L/R) scales (Chapieski et al., 2011). These scales consist of a smaller number of items. An average of the item responses from each scale was used in the present study. Cronbach's α was previously reported for a larger sample of children with epilepsy

(Chapieski et al., 2011). For the parent version the $\alpha = 0.90$ and 0.87 for the Prospective Memory and Learning/Retrieval scales and for the child version, $\alpha = 0.81$ and 0.73, respectively.

Academic measures. *Kaufman –Test of Educational Achievement – 2nd edition (K-TEA-II*; Kaufman, 2004) was used to assess academic skills. The Reading composite was composed of the Letter and Word Recognition and Reading Comprehension subtests. The Mathematic composite was composed of the Math Concepts & Applications, and Math Calculations subtests. Split-half reliability for the reading composite is $r = 0.97$ and $r = 0.96$ for the math composite. Two participants were missing the Math Calculations subtests; for these cases the Math Concepts & Applications score alone was utilized.

Analyses

Preliminary Analyses. Preliminary analyses addressed variable distributions, formation of composites of individual subtests, baseline group differences and evaluation of attrition, formation of pre-surgical and post-surgical z-scored analytic variables, and consideration of covariates.

Variables. Variable distributions were examined within and across groups, both graphically and statistically, in order to assess for the outliers. The Shapiro-Wilk test of normality was used for continuous variables. Additionally, the skewness and kurtosis of the variables were examined. Overall, the distributions of the variables approached normal with minimal outliers.

Composite Scores. For most of the analyses described below, composite scores were used. As there are relatively small sample sizes and multiple measures, using composite variables of related constructs should yield more reliable measures, and therefore help to decrease the probability of Type II error. Prior to creating these scores, correlations were performed with the baseline scores of all participants (*N*=102) to determine the strength of the relationships among subtests of proposed composites. Those correlations yielded significant relationships, $p < .05$; range $|r| = .28$ to .78, for the individual variables considered for each composite, with the exception of the variables contributing to the non-verbal memory and the everyday memory composites, as discussed below. Performances of the variables that made up each composite were averaged (all measures within any composite were on the same scale). Baseline performances were z-score standardized against the full sample of 102 with cognitive data, and follow-up composites were expressed relative to this same metric. A variety of approaches were considered (and yielded highly similar results), but this approach allowed both baseline and follow-up composite performances to be expressed as deviations from the entire eligible sample. As noted, those who did versus did not return for follow-up were highly similar, which meant that baseline values of the composites were very close to zero.

The most narrow composite scores (those created for hypotheses 3 and 4) were verbal immediate memory, verbal delayed memory, verbal recognition memory, non-verbal immediate memory, and non-verbal delayed memory. The verbal immediate memory variable was a composite of the WRAML-2 Story Memory, WRAML-2 Word List Learning, and TOMAL-2 Paired Recall. The range of correlations among these three variables at baseline and follow-up was $r = .28$ to .57, $p < .05$.This pairing of subtests is meaningful, as theWRAML-2 subtests contribute to the Verbal Memory Index of the WRAML-2 (Sheshlow & Adams, 2003) and the TOMAL-2 subtest contributes to the Verbal Memory Index of the TOMAL-2 (Reynolds & Voress, 2007). For the non-verbal memory composite score, the FM and VSR scores were not significantly correlated, $r = -.04$ to .16, $p > .05$) at either time point and there were considerable missing data for FM at baseline ($n = 13$). Therefore, the VSR score was used for the non-verbal immediate memory variable. However, as several facial memory measures have been cited often in the literature (Beardsworth & Zaidel, 1994; Gonzalez et al., 2012; Mabbott & Smith, 2003; Smith, Elliott, & Lach, 2004), some exploratory analyses were also conducted using FM in the smaller sample for comparison. The verbal delayed memory composite score included the Story Memory and List Learning delayed variables, $r = .28$ to $.44$, $p < .04$, and the non-verbal delayed memory composite was the VSR delayed task. The verbal recognition composite consisted of the Story Memory Recognition and List Learning Recognition, $r = .35$ to $.36$, $p < .001$).

In addition to those more narrow objective memory composite scores, broad composite scores were formed for hypotheses 1 and 2. These were created to help reduce the number of variables being analyzed as well as to provide structure for those hypotheses. All of the memory subtests were significantly related, $p < .05$. These composite scores included: 1) immediate memory (Story Memory, List Learning, Paired Recall immediate, and VSR immediate); 2) delayed memory (delayed components of Story Memory, List Learning, and VSR); 3) recognition memory (Story Memory and List Learning); and 4) objective memory (immediate, delayed, and recognition Story Memory, immediate, delayed, and recognition List Learning, immediate Paired Recall, and immediate and delayed VSR).

For the everyday memory composite score, the child and parent scores for each scale did not correlate at post-test (PM scale $r = .12$ and L/R scale $r = .26$; $p > .05$). The parent scales were used in the analyses as they were found to be more reliable than the child scales at baseline for this sample (PPM scale $\alpha = .88$ and PL/R scale $\alpha = .89$; CPM scale $\alpha = .77$ and CL/R scale $\alpha = .73$), as well as in the parent sample (reported in the Everyday Memory section above). The academic skills composite score was made up of the KTEA-II Reading Composite and the KTEA-II Math Composite.

Analyses for Hypotheses. Repeated measures ANOVAs was used for the primary hypotheses. Assumptions of repeated measures ANOVA, including independence, normality, and homogeneity of variance, were assessed (Field & Miles, 2010). Normality was assessed as described above. To test homogeneity of variance, Levene's test (Levene, 1960) was used to test the hypothesis that the variances in different groups are equal. Assumptions were not violated for any analyses. For each of the analyses reported below, time was the repeated (within subjects) factor, and group (seizure/surgery foci) was the between groups factor. Main effects of group and time, as well as the Group x Time interaction effects are reported. For hypotheses 1 through 4, when the Group x Time interactions were significant, follow-up paired t-tests were performed to evaluate whether individual subgroups declined or improved over time. In these cases, analyses were performed such that reported negative t-values indicated a decline in performance, whereas a positive t-value represented improvement.

The hypotheses proceeded from most general to most specific, both in terms of the groups contrasted, as well as the dependent measures (composite scores) utilized. Each hypotheses focuses on a specific two-group contrast; in each case, one of the groups corresponds to one of the five subgroups outlined above, whereas the other group is a combination of two or more of the surgical groups, except for hypothesis 4, which directly compared the L-TLE and R-TLE subgroups. Simultaneously, the dependent measures also became more specific across hypotheses. Given that the subgroups were unbalanced in their (small) sample size, and given that dependent measures varied across hypotheses, the most direct way to answer the questions posed by the hypotheses was to analyze pre-defined combinations of groups.

For hypotheses 1a, 1b, and 1c, the 2x2 repeated measures ANOVA design had the between subjects group factor (Surgery vs. No Surgery) was evaluated over time (baseline vs.

follow-up assessment) as the within subjects factor. All four surgery groups were collectively compared to the No Surgery control group as there were no differential hypotheses regarding the three primary outcomes: the broad composites of objective memory (1a), everyday memory (1b), and academic function (1c), with these composites described above.

For hypotheses 2a, 2b, and 2c, the repeated measures ANOVA again had time as the within subjects factor, and 2 groups for the between subject factor, where one group was a combined group consisting of the two TLE and FLE subgroups, and the other was the subgroup with non-temporal or non-frontal foci (the "Other" subgroup). Hypotheses 2a, 2b, and 2c utilized the same dependent measures as hypothesis 1 (corresponding to outcomes 1a, 1b, and 1c).

Hypothesis 3 also utilized a repeated measures ANOVA, again with time (baseline vs. follow-up assessment) as the within subjects factor, and a 2-level group as the between subject factor (one group consisted of the two TLE subgroups – left and right – and the other consisted of the FLE subgroup). Hypotheses 3a through 3e focused on different composite outcomes (several more narrow than hypotheses 1 or 2, each defined above): immediate memory (3a); delayed memory (3b); recognition memory (3c); everyday memory (3d); and academics (3e).

Hypothesis 4 also used a series of group (L-TLE vs. R-TLE) by time (baseline vs. follow-up assessment) repeated measures ANOVA. Hypotheses 4a through 4d focused on the following dependent measures: immediate verbal memory (4a); non-verbal immediate memory (4b); delayed verbal memory (4c); and non-verbal delayed memory (4d).

Hypothesis 5 added covariates to the models above where there were group, time, or Group x Time effects for a given dependent variable. Covariates were included if they were not strongly correlated with each other, if they did not interact with the group variables, and if they were strongly correlated with the dependent variables at baseline and follow-up. The L-TLE, R-

TLE, FLE, Other, and No Surgery groups were compared on demographic, other cognitive (IQ and language), and seizure-related variables, using analysis of variance (ANOVA). The demographic variables include age at baseline, mother's level of education, gender, and ethnicity. The seizure-related variables include number of medications and seizure frequency, age of onset, age of surgery, follow-up interval, and involvement of the hippocampus (IH; for the TLE groups). The change in seizure frequency variable was skewed (-3.87) and kurtotic (16.37), so it was analyzed as a dichotomous variable (seizure freedom at follow-up assessment). The means and standard deviations of these descriptive variables are reported in Table 3. Table 4 reports the individual variable means and standard deviations for the Surgery and No Surgery groups and Table 5 includes means and standard deviations for the four individual surgery groups at baseline and follow-up. There were no overall group differences on the other cognitive or demographic variables ($p > .05$), but the FLE and TLE groups differed on the number of seizures before surgery. The FLE group had a higher frequency, $p < .05$. The No Surgery group had a longer follow-up interval, $p < .05$, than the Surgery group and the R-TLE group had a longer follow-up interval than the L-TLE group, $p < .05$.

Pearson correlations were used for mother's education level, age of onset, age at surgery, follow-up interval, and change in medications (Maxwell & Delaney, 2004). Correlations with outcome variables were non-significant at both time points for most variables ($|r| = .002$ to .27) with the exception of the relation of age at surgery with non-verbal delayed memory at follow-up, $p < .05$, $r = .31$. The IH and seizure frequency variables were assessed using ANOVA. These ANOVAs also yielded non-significant relationships with the outcome variables, $p > .05$. As the goal was to address the impact of these variables in this population, seizure related variables were examined in children who significantly declined (defined as greater than 1 standard deviation change from baseline to follow-up testing) to determine potential differential patterns of performance.

Power and Effect Size. The small sample size per group can decrease power in the present study. However, the sample size of approximately 10 children per group is similar to, if not larger than, those in the current literature (Chieffo et al., 2010; Dlugos et al., 1999; Gonzalez et al., 2012; Hepworth & Smith, 2002; Lah et al., 2002; Lendt et al., 2002; Szabo et al., 1998; Williams et al., 1998) and significant differences have been reported. Additionally, effect sizes were also calculated. The proportion of variance explained by group differences was reported with partial eta-squared, η_p^2, computed as $[SS_{effect}/(SS_{effect} + SS_{error})]$. Cohen's d was another effect size, computed as $[(M_1 – M_2)/SD_{pooled}]$, and were used primarily to assess change over time. For the effect sizes reported below, a negative *d* indicates decline and a positive *d* indicates improvement.

Results

The first hypothesis compared the changes over time in composite scores of objective memory, everyday memory, and academic skills of children who had surgery and those who did not have surgery with three separate ANOVAs. The means and standard deviations for the individual variables for the Surgery and the No Surgery Groups are in Table 4. The means and standard deviations for the composite scores for the Surgery and the No Surgery Groups are reported in Table 6. For the objective memory composite score, the main effect of group was not significant, $F < 1.0$. The main effect of time (baseline to follow-up) was not significant, $F < 1.0$. The Group x Time interaction effect for the Surgery and No Surgery groups was also not significant, $F < 1.0$. This pattern of results indicates no systematic differences between the two groups evaluated here across time, but this does not preclude differences among individual surgical subgroups, which are evaluated below.

For the everyday memory composite score, the main effects of group (Surgery versus No Surgery) and time were not significant $F < 1.0$. There was also no Group x Time interaction, $F < 1.0$.

For the academic composite score, the main effect of group was not significant, $F(1,52) = 1.30$, $p > .05$. The effect for time was significant, $F(1,52) = 4.56$, $p < .04$. The interaction effect was also significant, $F(1,52) = 4.97$, $p < .04$, $\eta_p^2 = .09$. Follow-up t-test analyses of each group from baseline to follow-up showed that the No Surgery group significantly declined, $t = -2.82$, $p < .02$ ($d = -.37$) and there was no significant change in the combined Surgery group ($d = +.01$; see Figure 1).

Hypothesis 2 used the same composite variables to compare the combined FLE and TLE groups to the Other group. The means and standard deviations for the composite scores in scaled and z-scores for the FLE and TLE groups are reported in Table 7, with both the scaled score and z-scores provided. For the objective memory composite score, the main effect of group was not significant, $F < 1.0$. The main effect for time was also not significant, $F(1,42) = 2.64$, $p > .05$, suggesting no practice effects. However, the Group x Time interaction was significant, $F(1,42) = 4.92$, $p < .04$, $\eta_p^2 = .10$. See Figure 2. The changes over time were not significant for the combined TLE and FLE group, $t < 1.0$, $d = -.09$) or the Other group, $t = 1.97$, $p > .05$; however, the Other group showed a large effect size ($d = +0.84$).

For the everyday memory composite score, the main effects of group and time were not significant, both $F < 1.0$. As well, the interaction effect for the everyday memory composite was not significant, $F < 1.0$.

For the academic skill composite score, the main effects of group and time were not significant, both $F < 1.0$. The Group x Time interaction effect for these two groups was also not significant, $F < 1.0$.

Hypothesis 3 focused on change in combined TLE (R and L subgroups) relative to the FLE subgroup. The outcome measures included immediate and delayed memory (combined verbal and non-verbal), as well as recognition memory (only verbal recognition memory measures were available), everyday memory, and finally, academic skill. Means and standard deviations of the composite scores in scaled and z-scores are reported in Table 8.

For the immediate memory composite score, the main effects of group, $F < 1.0$, and time, $F(1,34) = 3.02$, $p > .05$) were not significant. The Group x Time interaction was significant, $F(1,34) = 24.72$, $p < .0001$, $\eta_p^2 = .42$. Follow-up t-tests revealed that the TLE group significantly declined, $t = -2.76$, $p < .02$; $d = -0.40$, while the FLE group significantly improved, $t = 6.63$, $p < .0001$; $d = +1.28$. See Figure 3.

For the delayed memory composite score, the main effects of group and time were not significant, both $F < 1.0$. The Group x Time interaction was significant, $F(1,34) = 15.89$, $p < .0004$, $\eta_p^2 = .32$. Follow-up t-tests for the groups of interest revealed that the TLE group significantly declined, $t = -3.40$, $p < .003$; $d = -0.40$, while the FLE group approached significant improvement, t = 2.19, $p = .056$; $d = +0.73$). See Figure 4.

Given the above pattern, follow-up analyses with these subgroups explored whether the results for immediate and delayed memory were consistent with regard to their verbal and non-verbal components, especially given that the memory composites contained more verbal than non-verbal measures. The results indicated that the Group x Time interactions remained significant, all $p < .03$, for immediate verbal ($\eta_p^2 = .30$), immediate non-verbal ($\eta_p^2 = .14$), and delayed verbal ($\eta_p^2 = .19$) composite scores with the TLE groups showing significant decline ($d = -0.38$, $d = -0.28$, $d = -0.41$, respectively) and the FLE group showing significant improvement ($d = +0.91$, $d = +0.45$, $d = +0.49$, respectively). The delayed non-verbal composite score did not show a significant Group x Time interaction, $p > .05$. When this analysis was performed using the TOMAL-2 Facial Memory, the Group x Time interaction was not significant for immediate memory, $F < 1.0$, or delayed memory, $F(1,19) = 1.11$, $p > .05$, although these analyses included only 21 of the 36 participants in these groups.

For the recognition memory composite score, the main effects for group, $F(1,32) = 1.60$, $p > .05$, and time, $F < 1.0$ were not significant. The Group x Time interaction was also not significant, $F < 1.0$.

For the everyday memory composite score, the main effects for group, $F(1,26) = 1.13$, $p > .05$, and time, $F < 1.0$ were not significant. The Group x Time interaction was also not significant, $F(1,26) = 2.83$, $p > .05$. Since the everyday memory questionnaire consisted of two separate scales, Prospective Memory (PM) and Learning/Retrieval (L/R), which could potentially differ in these groups (i.e. FLE decline in PM and TLE decline in L/R), follow-up analyses were conducted to address this. For PM, the main effects of group and time were not significant, both $F < 1.0$. The Group x Time effect was also not significant, $F < 1.0$. For L/R, the main effects of group and time were not significant, both $F < 1.0$. However, the Group x Time interaction was significant, $F(1,26) = 8.95$, $p < .007$, $\eta_p^2 = .26$. Follow up t-tests showed that the combined TLE group declined, $t = -2.56$, $p < .02$, $d = -0.31$, while the FLE group approached significant improvement, $t = 2.26$, $p = .059$, $d = +0.32$. See Figure 5.

For the academic composite score, the main effects of group and time were not significant, both $F < 1.0$. The Group x Time interaction was also not significant, $F < 1.0$.

Hypothesis 4 considered material specificity in the left and right TLE groups. The means and standard deviations of the composite scores (in standard/scaled and z-scores) are reported in Table 9. For the immediate verbal memory composite, the main effect of group was significant, $F(1,24) = 4.31, p < .05, \eta_p^2 = .15$, such that the R-TLE group performed better than the L-TLE group at baseline ($d = 0.75$) and follow-up ($d = 0.84$). The main effect of time was also significant, $F(1,24) = 6.31, p < .02, \eta^2 = .21$; effect sizes showed decreases in both groups over time (L-TLE $d = -0.65$, R-TLE $d = -0.50$). The Group x Time interaction was not significant, $F < 1.0$.

For the immediate non-verbal memory composite score, the main effects of group and time were not significant, $F < 1.0$ and $F(1,24) = 1.29, p > .05$, respectively. The Group x Time interaction was also not significant, $F < 1.0$. When these analyses were also conducted using the TOMAL-2 Facial Memory (immediate) subtest, the main effects of group, $F(1,15) = 2.51, p > .05$, and time, $F < 1.0$, were also not significant. The Group x Time interaction was also not significant, $F < 1.0$. As earlier noted, however, the sample size was severely reduced for this measure. Effect sizes were considered to elucidate possible differences between the two immediate non-verbal memory tasks. Both L- and R-TLE groups had negative effect sizes; for VSR, the effect sizes for the R-TLE and L-TLE group appeared similar, $d = -0.34$ and $d = -0.25$, respectively. For Facial Memory, the effect size was somewhat larger in the R-TLE group, $d = -0.53$, relative to the L-TLE group, $d = -0.12$.

For the delayed verbal memory composite score, the main effect of group was significant, $F(1,24) = 7.06, p < .02, \eta^2 = .23$. The main effect of time was also significant, $F(1,24) = 5.91, p < .03$. The Group x Time interaction was not significant, $F < 1.0$.

For the delayed non-verbal memory composite score, the main effects for group and time were not significant, $F(1,24) = 1.81, p > .05$ and $F < 1.0$, respectively. The Group x Time interaction was also not significant, $F < 1.0$. When these analyses were also conducted using the TOMAL-2 Facial Memory delayed subtest, the main effects of group and time were not significant, both $F < 1.0$. The Group x Time interaction was also not significant, $F < 1.0$. Effect sizes indicated that the L-TLE showed little change for VSR or Facial Memory, $d = -0.07$ and $d = +0.07$, whereas the effect size for the R-TLE group was larger for the Facial Memory task, $d = -0.41$, than for VSR, $d = -0.15$.

Hypothesis 5 considered the seizure-related and demographic variables (change in medications, seizure freedom at follow-up, age of onset, age at surgery, follow-up interval, maternal education, and surgical involvement of the hippocampus for TLE only; IH). As stated above only the TLE group ($n = 26$) evidenced decline for any of the outcome measures; therefore, those who declined the most within this group (> 1SD) were examined to identify variables related to decline. In regard to objective memory, level of change was examined in the following composite scores: verbal immediate (6 declined), verbal delayed (8 declined), non-verbal immediate (8 declined), and non-verbal delayed memory (4 declined) in order to more carefully assess the specific type of memory change. Since the Learning/Retrieval scale of the Everyday Memory questionnaire showed significant decline in the TLE group as compared to the composite everyday memory score, that variable was also used in the analysis, though only 2 children showed decline. Decline in the academic composite variable was also examined, though only one child significantly declined. Of the two children who declined on the L/R variable, one of the children also significantly declined on both immediate and delayed non-verbal memory variables and the other did not decline on other cognitive memory variables. Chi square analyses were used to assess differences between those who declined and those who did not within the TLE group for seizure freedom and IH. Results showed that the groups did not differ on those two seizure variables for any of the composite scores, $p > .05$. The comparison of who declined in the academic composite score and the L/R score could not be conducted due to the low number of children with TLE significantly declined. T-tests were used to explore group differences for change in medications, age of onset, age at surgery, mother's education, and follow-up interval. These results also did not reveal any group differences, all $p > .05$. The low N of course tempers these statistical results, though visual inspection is available via Table 10, where means, standard deviations, and chi-square analyses are reported.

Discussion

The purpose of this study was to determine the functional risks and benefits of surgical intervention for intractable epilepsy in children with TLE and FLE. Specifically, measures of objective memory, including immediate, delayed, and recognition as well as verbal and non-verbal, everyday memory, and academic skills were considered. Additionally, the impact of demographic and seizure-related variables – including seizure frequency at follow-up, change in medications, age at surgery, age of onset of seizures, follow-up interval, mother's level of education, and involvement of the hippocampus – was explored.

The results of this study did not reveal significant improvements or declines in either objective or subjective memory associated with surgery overall. However, the Surgery and No Surgery groups did differ on academics such that children who had surgery remained stable over time while those without surgery showed a decline in performance from pre- to post-assessment. Amongst the four surgery groups, as expected, the combined TLE and FLE group performed differentially over time on a composite of objective memory. While the change from baseline to follow-up was not statistically significant for either group, review of the effect sizes showed positive change over time for the Other group (*d* = +.84) relative to the combined TLE and FLE group (*d* = - .09). The groups did not differ over time on everyday memory or academic performance. When the objective measures were further broken into immediate, delayed, and recognition memory, results showed that the combined TLE groups declined significantly over time on measures of immediate and delayed memory while the FLE group improved. Even with this decline, the combined TLE group still performed within the low average range on immediate and delayed verbal memory (see Table 8). The two groups did not differ over time on recognition memory, everyday memory, or academic performance. Finally, findings from this study were consistent with studies showing a lack of material specific decline or improvement after surgery among the L- and R-TLE groups (Dlugos et al., 1999; Gleissner et al., 2002; Gonzalez, Mahdavi, Anderson, & Harvey, 2012; Jambaque et al., 2007; Mabbott & Smith, 2003; Szabo, et al., 1998; William et al., 1998). Both groups showed similar declines over time in verbal and non-verbal memory, though the R-TLE group generally outperformed the L-TLE group.

Objective Memory

The finding of a decline in the combined TLE group on immediate and delayed memory composite scores differs from much of the current literature that suggests this group will improve or remain unchanged following surgery (Beardsworth & Zaidel, 1994; Gleissner et al., 2002; Kuehn et al., 2002). However, some studies did find declines in immediate verbal memory (Szabo et al., 1998), delayed verbal memory (Szabo et al., 1998; Williams et al., 1998), and overall verbal memory (Dlugos et al., 1999). The current study similarly found that both immediate and delayed memory declined regardless of material specificity. These results replicate those reported from adult studies, which have found a decline in memory for the TLE group, though in that literature, laterality differences are often found as well (Frisk & Milner, 1990; Helmstaedter & Kockelmann, 2006; Sherman et al., 2011).

There are several possibilities for this decline within the TLE group. First, it is possible that other seizure-related variables influenced this result. For example, some research has shown that children perform better post-surgery if they have lower seizure frequency (Lendt et al., 1999) and are prescribed fewer medications (Hepworth & Smith, 2002; Mabbott & Smith, 2003). Interestingly, though, this was not the case in our study as both the R- and L-TLE groups experienced similar declines in seizures (Left: M = 16 to 2 and Right: M = 30 to 1, see Table 2), with 10 and 9 children experiencing seizure freedom, respectively. As well, the TLE group took fewer medications taken after surgery, averaging only one medication at that time, which did not differ significantly from the other groups. Meekes et al. (2013) found that children's memory scores were not significantly related to a reduction in number of medications until 24 months post-surgery. At this time, there was a significant number of children with no medications who performed better than children who continued medications. We, nevertheless, found memory declines at a shorter follow-up period despite good medical outcomes (decrease in seizures and medications).

Other research has shown that earlier age of onset of the seizure disorder negatively impacts performance after surgical intervention (Gleissner et al., 2002; Gonzalez et el., 2012; Jambaque et al., 2007; Mabbott & Smith, 2003). Although our groups did not significantly differ on age of onset, the L-TLE group (who showed clear declines) had the oldest age of onset (8 years) and therefore our results in this case do not support the age of onset hypothesis. Research regarding age at surgery has found that earlier age of surgery is associated with better outcomes in children (Jambaque et al., 2007; Westerveld et al., 2000). Again, the groups in the present study did not differ on this variable, although the L-TLE group did have the greatest age of surgery on average (15.35 years). However, when those who declined (> 1 SD) in the TLE group on the outcome variables were compared to those in the TLE group who did not decline, there was no difference between those subgroups on age at surgery. Further, children with R-TLE, who also evidenced decline, did not have an older age of surgery (*m* = 13.64 years) as compared with other groups in this study (total *m* = 13.83 years). Of the studies that identified declines, the Williams et al. (1998) and Dlugos et al. (1999) had an age of surgery similar to that of the current study while the Szabo et al. (1998) had a younger age of surgery (9.4 years). Seven of the 13 studies that showed improvement or remained unchanged had younger ages of surgery (<12 years). Therefore there is some evidence that older age of surgery negatively impacts performance, though this would not explain why the TLE group differentially declined more than the other groups in our study that had a similar age of surgery.

As mentioned previously, studies with shorter follow-up intervals (<6 months) tend to find decline in objective memory (Gleissner et al., 2002; Lah et al., 2002; Szabo et al., 1998), with evidence of subsequent improvement if also assessed at a later time point (Gleissner et al., 2002). In the current study there was a significant group difference in follow-up intervals such that the L-TLE group had a significantly shorter interval (18 months) than the FLE (28 months) and No Surgery (33 months) groups. One child in the L-TLE group had a much shorter follow-up interval (6 months). However, that child actually improved overall, with the exception of non-verbal immediate memory, and the improvement suggests that the shorter interval likely did not disproportionately influence the overall decline seen in the L-TLE group. Further, the R-TLE group, which also declined, also had a long follow-up interval (27 months). When children in the

TLE group who declined more than 1 standard deviation were compared with those who did not, these groups did not differ on follow-up interval. The results of existing studies suggest that a stable cognitive profile is evident by 12 months post-surgery Therefore, since the groups in the current study all had a mean follow-up interval of over one year, it is unlikely differences in follow-up interval fully explain differences in performance.

It has been suggested that children who have higher memory scores at baseline testing show a greater decline at follow-up (Dlugos et al., 1999; Szabo et al., 1998). This pattern has also been observed in adults with TLE. For example, Chelune and colleagues found that higher pre-operative performance in L-TLE patients resulted in greater decline, while there was no consistent relationship in the R-TLE group (Chelune, Naugle, Luders, & Awad, 1991). In the present study, the baseline scores on objective memory measures in the L-TLE group were at or below the overall mean of the five groups, whereas the R-TLE group scores were above that average and showed a similar decline to the L-TLE group. Our findings are consistent with the Meekes et al. (2013) study which also did not find that a higher score at baseline testing was related to a greater decline in their patients with L-TLE. Therefore, it does not seem likely that the declines shown here in the combined TLE group can be attributed to a higher ability at baseline.

We also considered parental level of education as an explanatory factor. In the current study the groups were compared on mother’s level of education and were not found to differ. Further, when the TLE group who declined significantly was compared to those who did not, the groups again did not differ on this variable suggesting this did not have an impact on decline following surgery.

Lastly, research with adults has also shown that those with surgical intervention involving the mesial temporal lobe (i.e., hippocampus) perform worse on measures of memory (Gleissner et al., 2002) due to the involvement of the hippocampus in the formation of new memories (Loring & Meador, 2003). However, patients who had damage to the hippocampus prior to surgery (e.g. MTS) may actually show less decline in memory than those without hippocampal damage and therefore other etiologies of seizures, such as tumors or dysplasia, may result in greater declines in memory (Adams et al., 1990; Chelune, Kneebone, Dinner, Awad, & Naugle, 1993). In the current study, six of the children with L-TLE had MTS and one of the children in the R-TLE group did. The majority of the remaining children had either a tumor or cortical dysplasia. Of the 26 children in the combined TLE group, 17 had a mesial temporal lobe resection (Left – 11, Right – 6). This would suggest that 9 children (Left – 4, Right – 5) potentially had a relatively intact hippocampus prior to surgery as there was no evidence of MTS. This may account for some of the memory decline seen in this group. While there was no group difference between those that did and did not have mesial temporal involvement prior to surgery, 5 of the 9 children with relatively intact hippocampi evidenced significantly decline on at least two of the objective memory measures.

In sum, the results of this study show that surgical resection of the temporal lobe may negatively impact performance on objective measures of immediate and delayed verbal memory independent of a number of seizure related variables. Of note, many of the children in this study had an etiology other than MTS, such as cortical dysplasia or tumor, which may have contributed to the observed decline in memory. The findings suggest that, even if children have a better recovery following a temporal lobectomy than adults, the functions of the temporal lobe are not entirely compensated for by other regions of the brain.

Our results differ from many other studies, which have found unchanged or improved memory function following surgical intervention in children with TLE. Another way to consider the current findings is in the context of task specificity rather than material specificity. Task specificity suggests that memory in the temporal lobe is organized by differences in the tasks, such as whether the information to be retained is semantically related versus unrelated, rather than only whether the information is verbal versus non-verbal (Saling, 2009). The task specificity model also proclaims that there is not unity within the clinical tests of verbal and non-verbal memory that are currently used in studies of epilepsy. This is an assumption of the material specificity model, and this lack of unity would be evidenced by variable performance by task (i.e. immediate memory vs. delayed) or type (i.e. unrelated word list learning vs. story memory) in patients with TLE. This is evident in our study. For example, for the non-verbal memory domain, at least in terms of effect sizes, the R-TLE group evidenced more decline on the Facial Memory task (immediate and delayed, $d = -.53$ and $d = -.41$, respectively), than on the VSR task (immediate and delayed, $d = -.34$ and $d = -.15$, respectively), although conclusions are tenuous given the small sample size for the Facial Memory task. However, results may be attributed to the familiarity of faces and their ability to be associated more easily with previously learned information than an array of dots. Within the verbal domain, the combined TLE group declined on the Story Memory (immediate and delayed) and the Verbal Learning (immediate and delayed) tasks. However, again looking at effect sizes, the decline was greater on the immediate and delayed trials of the Verbal Learning measure, $d = -.48$ and $d = -.61$, respectively, than on the Story Memory measure, $d = -.15$ and $d = -.18$, respectively. The task specificity model presents two models, a mesial protosemantic component and a lateral semantic component (Saling, 2009). The mesial component is involved with arbitrary paired associate learning while the lateral component is involved with memory of tasks that are semantically structured (e.g. passages; Saling, 2009). This shows that replication studies that continue to control for this extent of seizure-related variables as well as consider task specificity will be important in understanding our current findings within the context of the literature and the task specificity model.

Our study was consisted with the literature that shows improvement or unchanged performance in objective memory post-surgery for FLE patients (Chieffo et al., 2011; Lendt et al., 2002). As the FLE did not differ from the other groups on the demographic and seizure-related variables, it is less likely their performance was significantly impacted by these factors. When considering the etiology of seizures within the FLE group, most (7 of 10) had cortical dysplasia. While studies of cognitive outcomes following FLE surgery have not specifically considered etiology, research has shown a high rate of seizure freedom with this etiology (Hauptman & Mathern, 2012). As good seizure control is correlated with better cognitive outcomes, it is possible that this contributes to their improvement/unchanged scores in the present study.

Everyday Memory and Academic Function

While it is important to understand performance on objective measures, another important factor when considering outcomes following surgical intervention is the implication changes in cognition have on everyday functioning. Therefore, this study also investigated the impact of surgery on everyday measures, including everyday memory and academic skills. The current findings suggest that the decline seen in verbal immediate and delayed memory does not necessarily correspond to deficits in everyday memory as only two children declined in everyday memory with only one showing decline in cognitive memory as well (non-verbal only). These findings appear to support the results of previous studies (Sawrie et al., 1999; Smith, Elliott, & Lach, 2006). We, however, conducted additional analyses, separating the subjective memory measure into the learning/retrieval and prospective memory scales. These analyses revealed a decline in parent reports of learning/retrieval in everyday situations and this decline, like the results from the analyses with objective measures, was evident for the temporal lobe and not the frontal lobe group. In this case, the results showed that the TLE group declined significantly, $d = -0.31$, and the FLE group approached significant improvement, $d = 0.32$. Although one might expect a decline in prospective memory in the frontal lobe group, we did not find that to be the case in our sample. The failure of other studies to find an impact of temporal lobe resection on subjective reports of everyday memory may reflect the fact that the questionnaires employed heavily reflect prospective memory.

Regarding academic skills, the No Surgery group evidenced a decline while the Surgery groups remained grossly unchanged in academic skills suggesting that not only are the deficits in verbal memory not significantly impacting academics, but that the surgical intervention may have helped with everyday functioning in this regard. The only study to assess academics over time, Williams et al. (2002), focused on achievement tests rather than measures of school performance and found that most academic skills were in the average range prior to surgery, with math skills in the low average range, and no significant decline. In the current study, most groups performed in the average range on math and reading skills at baseline, with the exception of reading in the L-TLE group (low average) and math skills in the No Surgery group (low average). Similar to the aforementioned study, there was no evidence of decline in the surgery groups. It is possible that other factors contributed to this difference in the Surgery and No Surgery groups. For example, attention may be a mediating factor in a child's ability to adequately progress academically. Those in the No Surgery group may exhibit poor attention during school which in turn effects their acquisition of new academic skills, while attention may have improved in the Surgery group allowing them to continue to progress. Improvements in attention would, presumably, be due to decreases in seizure frequency or anticonvulsant medication.

Limitations

There are some limitations to this study. First, although our sample size is larger than many studies in the literature, it is still a small sample size. However, we did have statistically significant findings in the study suggesting the results are robust even with this limitation of power. There were results that approached significance (i.e. with comparisons of L-TLE and R-TLE) that may be significant with larger sample sizes and more power. Also, it is difficult to assess non-verbal memory (secondary to a wide variety of non-verbal tests used in the literature and difficulty finding a test of memory that does not inadvertently include a verbal component) and this may be responsible for the lack of differences in changes over time between the L- and R-TLE groups.

The literature has shown that children with more severe symptoms of epilepsy often also have more psychosocial concerns (Austin et al., 2010) and poor adaptive functioning (Papazoglou, King, & Burns, 2010). This was not assessed in the current study and it is possible that children in the TLE groups experienced concerns in these areas, which may have impacted their memory performance. However, Dlugos et al. (1999) reported that families expressed satisfaction with the intervention despite declines suggesting that decreased verbal memory is preferable to intractable seizures and therefore it is less likely that psychosocial or adaptive concerns would have that impact in the current study.

While academic achievement was assessed in the current study, it is still possible that children are experiencing difficulties in the classroom that impact performance in school that is not captured by the achievement tests. Therefore, comparing actual reported grades in school may be more sensitive in showing changes in school performance over time. Additionally, it is also possible that behavior in school may change which could be evaluated via teacher report. Another limitation is related to the seizure-related variables. While our study included many seizure related variables, dosage of mediations and the extent of the resection were not assessed. Gleissner and colleagues (2002) suggest that the larger extent of resection in their study led to greater seizure freedom, but this was at the expense of greater verbal memory decline at 3-months post-surgery. As well, though age at surgery was considered in this study, data were not available regarding pubertal status at surgery. While pubertal status per se does not necessarily influence seizure activity, hormonal levels may play a role in the frequency of seizures which may in turn impact cognition (Wheless & Kim, 2002).

Summary

The results of this study suggest that children who have surgical intervention for L- or R-TLE may experience a decline in immediate and delayed verbal memory, from the average range to the low average range overall; non-verbal memory appears generally unchanged. Of the demographic and seizure-related variables that were assessed in this study, only the etiology (i.e. MTS or other) may have impacted the results such that those with an etiology other than MTS that had surgery within the mesial temporal lobe tended to show decline on cognitive memory measures. The study also considered the functional consequences of changes in verbal memory and found that academic and everyday memory performance was grossly unchanged, although parents were aware of a decline in their child's ability to learn and retrieve information in their everyday lives. Therefore, families of children who are candidates for surgical intervention in the temporal lobe should consider the possibility of a decline in verbal memory. However, there does not appear to be significant functional impairments in academic skill as a result. Though the declines occur in objective memory for the TLE group, there was evidence for positive outcomes including decrease in seizure frequency and reduction in seizure medications, as well as either improvement or relatively unchanged performed in the FLE and Other groups.

References

Achenbach, T.M. (1991) Manual for the Child Behavior Checklist/4-18 and 1991 profile. Burlington:Department of Psychiatry, University of Vermont.

Adachi, N., Kanemoto, K., Muramatsu, R., Kato, M., et al. (2005). Intellectual prognosis of status epilepticus in adult epilepsy patients: Analysis with Wechsler Adult Intelligence Scale –Revised. *Epilepsia, 46 (9),* 1502-1509.

Allegri, R.F., Drake, M., & Thomson, A. (1999). Neuropsychological findings in patients with middle temporal lobe epilepsy. *Review Neurology, 29*, 1160-1163.

Austin, J.K, Perkins, S.M., Johsnon, C.S., Fastenau, P.S., Byars, A.W., deGrauw, T.J., & Dunn, D.W. (2010). Self-esteem and symptoms of depression in childrne with seizures: Relationships with neuropsychological functioning and family variables over time. *Epilepsia, 51(10),* 2074-2083.

Baldo, J.V. & Shimamura, A.P. (2002). Frontal Lobes and Memory. In Baddeley, A., Wilson, B., & Kopelman, M. (Eds.), *Handbook of Memory Disorders 2nd Edition*. John Wiley & Co.: London.

Baldo, J.V., Delis, D., Kramer, J., & Shimamura, A.P. (2002). Memory performance on the California Verbal Learning Test II: Findings from patients with focal frontal lesions. *Journal of the International Neuropsychological Society, 8,* 539–546.

Baxendale, S., Hearney, D., Thompson, P.J., & Duncan, J.S. (2010). Cognitive consequences of childhood-onset temporal lobe epilepsy across the adult lifespan. *Neurology, 75,* 705-711.

Baxendale, S. & Thompson P. (2005) Defining meaningful postoperative change in epilepsy surgery patients: Measuring the unmeasurable? *Epilepsy Behavior, 6,* 207–11.

Berg, A.T., Mathern, G.W., Bronen,R.A., Fulbright, R.K., DiMario, F., Testa, F.M., & Levy, S.R. (2009). Frequency, prognosis and surgical treatment of structural abnormalities seen with magnetic resonance imaging in childhood epilepsy. *Brain, 132,* 2785–2797.

Black, L.C., Schefft, B.K., Howe, S.R., Szaflarski, J.P., Yeh, H.S., & Privitera, M.D. (2010). The effect of seizures on working memory and executive functioning performance. *Epilepsy Behavior, 17,* 412-419.

Bjornaes, H., Stabell, K., Henriksen, O., & Loyning, Y. (2001). The effects of refractory epilepsy on intellectual functioning in children and adults: A longitudinal study. *Seizure, 10,* 250-259.

Bourgeois, B.F.D., Prensky, A.L., Palkes, H.S., Telent, B.K., & Busch, S.G. (1983). Intelligence in epilepsy: A prospective study in children. *The Annals of Neurology, 14,* 438 – 444.

Brown, M.W. & Aggelton, J.P. (2001) Recognition memory: What are the roles of the perirhinal cortex and hippocampus? *Nature Reviews Neuroscience*, *2*, 51–61.

Buckmaster, C.A., Eichenbaum, H., Amaral, D.G., Suzuki, W.A., & Rapp, P.R. (2004). Entorhinal cortex lesions disrupt the relational organization of memory in monkeys. *The Journal of Neuroscience, 24,* 9811 – 9825.

Cavazutti, V., Winston, K., Baker, R., & Welch, K. (1980). Psychological changes following surgery for tumours in the temporal lobe. *Journal of Neurosurgery, 53,* 618-626.

Chapieski, L., Evankovich, K., Hiscock, M., & Collins, R. (2011). Everyday verbal memory and pediatric epilepsy. *Epilepsy & Behavior , 21*, 285-290.

Chelune, G.J., Kneebone, A.C., Dinner, D.S., Awad, I.A., & Naugle, R.I. (1993). Contributions of the IAP and baseline neuropsychological testing in predicting memory outcome following epilepsy surgery: Further support for the "functional adequacy" model of hippocampal function [Abstract]. *Journal of Clinical and Experimental Neuropsychology, 15,* 24.

Chelune, G.J., Naugle, R.I., Hermann, B.P. et al. (1998). Does presurgical IQ predict seizure outcome after temporal lobectomy? Evidence from the Bozeman Epilepsy Consortium. *Epilepsia, 39 (3),* 314-318.

Chelune, G.J., Naugle, R.I., Luders, H., & Awad, I.A. (1991). Prediction of cognitive change as a function of preoperative ability status among temporal lobectomoy patients seen at 6-month follow-up. *Neurology,*

Chieffo, D., Lettori, D., Contaldo, I., Perrino, F., Graziano, A., Palermo, C., et al. (2011). Surgery of children with frontal lobe lesional epilepsy: Neuropsychological study. *Brain & Development , 33*, 301-315.

Chovas, R.J., McLachlan, R.S., Derry, P.A. & Cummings, A.L. (1994). Psychosocial function following temporal lobectomy: Influence of seizure control and learned helplessness. *Seizure, 3,* 171-176.

Cohen, J. (1988). *Statistical power analysis for the behavioural sciences* (2nd edition). New York: Academic Press.

Cohen, M. (1992). Auditory/verbal and visual/spatial memory in children with complex partial seizures of temporal lobe origin. *Brain and Cognition, (20),* 315-326.

Corcoran, R. & Upton, D. (1993). A role for the hippocampus in card sorting. *Cortex, 29,* 293-304.

Conners, C.K. (Ed.) (2004). Conners' Continuous Performance Test-2nd edition:version 5 for Windows: technical guide and software manual. North Tonawanda, NY: Multi-Health Systems.

Culhane-Shelburne, K., Chapieski, L., Hiscock, M., & Glaze, D. (2002). Executive functions in children with frontal and temporal lobe epilepsy. *Journal of the International Neuropsychological Society, 8,* 623-632.

DeCarlo, L.T. (1997). On the meaning and use of kurtosis. *Psychological Methods, 2(3),* 292-307.

Delaney, R.C., Rosen, A.J., Mattsen, R.H. & Novelly, R.A. (1980). Memory function in focal epilepsy: A comparison of non-surgical, unilateral temporal lobe and frontal lobe samples. *Cortex, 16(1),* 103-117.

Delis, D.C., Kaplan, E. & Kramer, J.H. (2001). Delis Kaplan Executive Function System (D-KEFS). The Psychological Corporation, San Antonio, TX.

Dennis, M., Farrell, K., Hoffman, H.J., Hendrick, E.B., Becjer, L.E., & Murphy, E.G. (1988). Recognition memory of item, associative and serial order information after temporal lobectomy for seizure control. *Neuropsychologia, 26,* 53-65.

Dickson, J.M., Wilkinson, I.D., Howell, S.J.L., Griffiths, P.D., et al. (2006). Idiopathic generalized epilepsy: A pilot study of memory and neuronal dysfunction in the temporal lobes, assessed by magnetic resonance spectroscopy. *Journal of Neurology, Neurosurgery and Psychiatry, 2,* 20 – 27.

Dlugos, D.J., Moss, E.M., Duhaime, A.C., & Brooks-Kayal, A.R. (1999). Language-related cognitive declines after left temporal lobectomy in children. *Pediatric Neurology, 21,* 444-449.

Drysdale, K., Shores, A., & Levick, W. (2004). Use of everyday memory questionnaire with children. *Child Neuropsychology, 10(2),* 67-75.

Dodrill, C.B. (2004). Neuropsychological effects of seizures. *Epilepsy & Behavior, 5,* S21-S24.

Dodrill, C.B. & Wilensky, A.J. (1990). Intellectual Impairment as an outcome of status epilepticus. *Neurology, 40(2),* 23-27.

Dunn, L. M., & Dunn, L. M. (2007a). Peabody Picture Vocabulary Test (4th ed.). Bloomington, MN: Pearson Assessments.

Dunn, L. M., & Dunn, L. M. (2007b). Peabody Picture Vocabulary Test (4th ed.): Examiner's manual. Bloomington, MN: Pearson Assessments.

Ellenberg, J.H., Hirz, D.G., & Nelson, K.B. (DO seizures in children cause intellectual deterioration? *New England Journal of Medicine, 314,* 984-1085.

Everts, R., Harvey, S. A., Lillywhite, L., Wrennall, J., Abbott, D. F., Gonzalez, L., et al. (2010). Language lateralization correlates with verbal memory performance in children with focial epilepsy. *Epilepsia , 51* (4), 627-638.

Field, A. & Miles, J. (2010). Discovering statistics using SAS. Sage Publication Inc., London.

Giovagnoli, A.R. (2001). Relation of sorting impairment to hippocampal damage in temporal lobe epilepsy. *Neuropsychologia, 39,* 140 – 150.

Giovagnoli, A.R., Mascheroni, S. & 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.

Gleissner, U., Kuczaty, S., Clusmann, H., Elger, C., & Helmstaedter, C. (2008). Neuropsychological results in pediatric patients with epilepsy surgery in the parietal cortex. *Epilepsia, 49*(4), 700-704.

Gleissner, U., Sassen, R., Lendt, M., Clusmann, H., Elger, C.E. & Helmstaedter, C. (2002). Pre- and postoperative verbal memory in pediatric patients with temporal lobe epilepsy. *Epilepsy Research, 51,* 287-296.

Gleissner, U., Sassen, R., Schramm, J., Elger, C.E., & Helmstaedter, C. (2005). Greater functional recovery after temporal lobe epilepsy surgery in children. *Brain, 128,* 2822-2829.

Glosser, G., Cole, L.C., French, J.A., et al. (1997). Predictors of intellectual performance in adults with intractable temporal lobe epilepsy. *Journal of the International Neuropsychological Society, 3 (3),* 252 – 359.

Gonzalez, L.M., Anderson, V.A., Wood, S.J., Mitchell, L.A., Heinrich, L. & Harvey, A.S. (2008). The Observer Memory Questionnaire – Parent Form: Introducing a new mearuse of everyday memory for children. *Journal of the International Neuropsychological Society, 14,* 337-342.

Gonzalez, L.M., Mahdavi, N., Anderson, V.A., & Harvey, A.S. (2012). Changes in memory function in children and young adults with temporal lobe epilepsy: A follow-up study. *Epilepsy & Behavior, 23,* 213-219.

Gulgonen, S., Demirbilek, V., Korkmaz, B., Dervent, A. (2000). Neuropsychological functions in idiopathic occipital lobe epilepsy. *Seizure, 41,* 405 – 411.

Hannay, H.J., Howieson, D.B., Loring, D.W., Fischer, J.S., & Lezak, M.D. (2004). Neuropathology for Neuropsychologists. In Lezak, M.D., Howieson, D.B., & Loring, D.W. (Eds). *Neuropsychological Assessment 4th Edition,* (pp. 157 – 193). London: Oxford University Press.

Hauptman, J.S. & Mathern, G.W. (2012). Surgical treatment of epilepsy associated with cortical dysplasia: 2012 update. *Epilepsia, 53(4),* 98-104.

Hauser, W.A. & Hesdorffer, D.C (1990). Epilepsy: Frequency, causes, and consequences. New York, NY: Demos Publications.

Helmstaedter, C., Gleibner, U., Zentner, J., & Elger, C. (1997). Neuropsychological consequences of epilepsy surgery in frontal lobe epilepsy. *Neuropsychologia , 36* (4), 333-341.

Helmstaedter, C., Grunwald, T., Lehnertz, K., Gleibner, U., & Elger, C. (1997). Differential involvement of left temporolateral and temporomesial structures in verbal declarative learning and memory: Evidence from temporal lobe epilepsy. *Brain and Cognition, 35,* 110-131.

Helmstaedter, C., Richter, S., Roske, S., Oltmanss, F., Shramme, J., & Lehmann, T. (2008). Differential effects of temporal pole resection with amygdalohippocampectomy versus selective amygdalohippocampectomy on material-specific memory in patients with mesial temporal lobe epilepsy. *Epilepsia, 49(1),* 88-97.

Helmstaedter, C., & Kockelmann, E. (2006). Cogntive outcomes in patients with chronic temporal lobe epilepsy. *Epilepsia, 47* (2), 96 – 98.

Hepworth, S. & Smith, M.L. (2002). Learning and recall of story content and spatial location after unilateral temporal-lobe excision in children and adolescents. *Child Neuropsychology, 8* (1), 16-26.

Hernandez, M., Sauerwein, H.C., Jambaque, I., de Guise, E., Lussier, F., Lortie, A., Dulac, O., & Lassonde, M. (2001). Neuropsychology of frontal lobe epilepsy. In Jambaque, I., Lassonde, M., & Dulac, O. (Eds.), *Neuropsychology of Childhood Epilespy,* (pp. 103-112). Hingham, MA: Kluwer Academic Publishers.

Hernandez, M., Sauerwein, H.C., Jambaque, I., de Guise, E., Lussier, F., Lortie, A., Dulac, O., & Lassonde, M. (2003). Attention, memory, and behavioral adjustment in children with frontal lobe epilepsy. *Epielspy & Behavior, 4,* 522-536.

Hermann, B.P., Seidenberg, M., & Jones, J. (2008). The neurobeahvioral comorbidities of epilepsy: Can a natural history be developed? *The Lancet Neurology, 7,* 151-60.

Hermann, B.P., Wyler, A.R., & Rickey, E.T. Wisconsin Card Sorting Test performance in patients with complex partial seizures of temporal lobe origin. *Journal of Clininical and Experimental Neuropsychology,10,* 467–476.

Jambaque, I., Dellatolas, G., Dulac, O., Ponsot, G., & Signoret, J. (1993). Verbal and visual memory impairment in children with epilepsy. *Neuropsychologia, 31(12),* 1331-1337.

Jambaque, I., Dellatolas, G., Fholen, M., Bulteau, C., Watier, L., Dorfmuller, G., et al. (2007). Memory functions following surgery for temporal lobe epilepsy in children. *Neuropsychologia , 45*, 2820-2862.

Jones-Gotman, M. Zatorre, R.J., Olivier, A., Andermann, F., Cendes, F., Staunton, H., McMackin, D., Siegel, A., & Wieser, H. (1996). Learning and retention of words and designs following excision from medial or lateral temporal-lobe structures. *Neuropsychologia, 35 (7),* 963-973.

Kadis, D.S., Stollstroff, M., Elliott, I., Lach, L., & Smith, M.L. (2004). Cognitve and psychological predictors of everyday memory in children with intractible epilepsy. *Epilepsy Behavior, 5,* 37 – 43.

Kaufman, A. Kaufman Test of Educational Achievement – 2nd edition: Manual (2004). Circle Pines, MN: American Guidance Service.

Kemper, B., Helmstaedter, C., Holinka, B., & Elger, C.E. (1992). Kognitive profile von praechirurgischen patienten mit Frontal- und Tem- porallappenepilepsie, In Scheffner D, (Ed.) *Epilepsie* (pp. 345–50), Reinbeck: Einhorn-Presse Verlag.

Kernan, C.L., Asarnow, R., Siddarth, P., Gurbani, S., Lanphier, E.K., Sankar, R., & Caplan, R. (2012). Neurocognitive profiles in children with epilepsy. *Epilepsia, 53(12),* 2156–2163.

Korkman, M., Granstrom, M., Kantola-Sorsa, E., Gaily, E., Paetau, R., Liukkonen, E., et al. (2005). Two-year follow-up of intelligence agter pediatric epilepsy surgery. *Pediatric Neurology , 33* (3), 173-178.

Kuehn, S.M., Keene, D.L., Richards, P.M.P., & Ventureyr, E. C.G. (2002). Are there changes in intelligence and memory functioning following surgery for the treatment of refractory epilepsy in childhood? *Child's Nervous System, 18,* 306-310.

Kwan, P. & Brodie, M.J. (2001). Neuropsycholgical effects of epilepsy and antiepileptic drugs. *Lancet, 357 (9251),* 216-222.

Lah, S. (2004). Neuropsychological outcome following focal cortical removal for intractable epilepsy in children. *Epilepsy & Behavior , 5*, 804-817.

Lee, T.M.C., Yip, J.T.H., & Jones-Gotman, M. (2002). Memory deficits after resection from left or right anterior temporal lobe in humans: A meta-analytic review. *Epilepsia, 43* (3), 283-291.

Lendt, M., Gleissner, U., Helmstadter, C., Sassen, R., Clusmann, H. & Elger, C.E. (2002). Neuropsychological outcome in children after frontal lobe epilepsy surgery. *Epilepsy & Behavior, 3,* 51-59.

Lendt, M., Helmstaedter, C., & Elger, C.E. (1999). Pre- and postoperative neuropsychological profiles in children and adolescents with temporal lobe epilepsy. *Epilepsia, 40* (11), 1543-1550.

Leunen, D., Caroff, X., Chmura, S., Fohlen, M., Delalande, O., & Jambaque, I. (2009). Verbal and spatial learning after temporal lobe excisions in children: An adaptation of the Grober and Buschke procedure. *Epilepsy Behavior , 16* (3), 534-538.

Levene, H. (1960). Robust tests for equality of variances. In I. Olkin, S.G. Ghurye, W. Hoeffding, W.G. Madow & H.B. Mann. (Eds.) *Contributions to probability and statistics: Essays in honor of Harold Hotelling,*(pp. 278 – 292). Standford, CA: Stanford University Press.

Lewis, D.V., Thompson, R.J., Santos, C.C., Oakes, W.J., Radtke, R.A., Friedman, A.H., Lee, N., & Swartzwelder, H.S. (1996). Outcome of temporal lobectomy in adolescents. *Journal of Epilepsy, 9,* 198-205.

Lippe, S., Bulteau, C., Dorfmuller, G., Audren, F., Delalande, O., & Jambaque, I. (2010). Cognitive outcome of parietooccipital resection in children with epilepsy. *Epilepsia* .

Loring, D.W. & Meador, K.J. (2003). Neuropsychological Aspects of Temporal Lobe Epilepsy Surgery. In Feinberg, T.E. & Farah, M.J. (Eds.), *Behavioral Neurology & Neuropsychology* (pp. 695-708). New York, NY: McGraw-Hill Companies, Inc.

Mabbott, D., & Smith, M. (2003). Memory in children with temporal or extra-temporal excisions. *Neuropsychologia , 41*, 995-1007.

Mateer, C.A. & Williams, D. (1991): Effets of frontal lobe injury in childhood. *Developmental Neuropsychology, 7,* 359-376.

Maxwell, S.L. & Delaney, H.D. (2004). Designing experiments and analyzing data, 2nd ed. Taylor & Francis Group: New York.

McDonald, C.R., Delis, D.C., Norman, M.A., Tecoma, E.S., & Iragui-Madozi, V.I. (2005). Is impairment in set-shifting specific to frontal-lobe dysfunction? Evidence from patients with frontal-lobe or temporal lobe epilepsy. *Journal of the International Neuropsychological Society, 11,* 477-481.

Meekes, J., Braams, O., Braun, K.P.J., Jennekens-Schinkel, A., van Nieuwenhuizen, O., on behalf of the Dutch Collaborative Epilepsy Surgery Programme (2013). Verbal memory after epilepsy surgery in childhood. *Epilepsy Research, 107,* 146-155.

Meyer, F., marsh, W.R., Laws, E.R., & Sharbrough, F.W. (1986). Temporal lobectomy in children with epilepsy. *Journal of Neurosurgery, 64* (3), 371-376.

Milner, B., Petrides, M., & Smith, M.L.(1985) Frontal lobes and temporal organization of memory. *Human Neurobiology, 4,* 137–42.

Miranda, C. & Smith, M.L. (2001). Predictors of intelligence after temporal lobectomy in children with epilepsy. *Epilepsy Behavior, 2* (1), 13 – 19.

Mizrahi, E.M., Kellaway, P., Grossman, R.G., et al. (1990) Anterior temporal lobectomy and medically refractory temporal lobe epilepsy of childhood. *Epilepsia, 31,* 302-312.

Nolan, M.A., Redblado, M.A., Lah, S., Sabaz, M., Lawson, J.A., Cunningham, A.M., Bleaset, A.F. & Bye, A.M.E. (2004). Memory function in childhood epilepsy syndrome. *Journal of Paediatrics and Child Health, 40*, 20 – 27.

Nolan, M.A., Redblado, M.A., Lah, S., Sabaz, M., Lawson, J.A., Cunningham, A.M., Bleaset, A.F. & Bye, A.M.E. (2003). Intelligence in childhood epilepsy syndromes. *Epilepsy Research, 53,* 139-150.

Oostrom, K.J., Smeets-Schouten, A., Kruitwagen, C.L.J.J., Peters, A.C.B., & Jennekens-Schinkel, A. (2003). Not only a matter of epilepsy: Early problems of cognition in children with “epilepsy only” – a prospective study starting at diagnosis. *Pediatrics, 112,* 1338-1344.

Oyegbile, T.O., Dow, C., & Jones, J., et al. (2004). The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. *Neurology, 62,* 1736-1742.

Papazoglou, A., King, T., & Burns, T. (2010). Active seizures are associated with reduced adaptive functioning in children with epilepsy. *Seizure, 19(7),* 409-413.

Reilly, C. & Neville, B.G.R. (2011). Academic achievment in children with epilepsy: A review. *Epilepsy Research, 97,* 112-123.

Reynolds, C. & Voress, (2007). Test of Memory and Learning – 2nd ed. Austin, TX: PRO-ED.

Risse, G.L. (2006). Cognitive outcomes in patients with frontal lobe epilepsy. *Epilepsia, 47* (2), 87-89.

Roulet-Perez, E., Davidoff, V., Mayor-Dubois, C., Maeder-Ingvar, M., Seeck, M., Ruffieux, C., et al. (2010). Impact of severe epilepsy on development: Recovery potential after successful early epilepsy surgery. *Epilepsia , 51* (7), 1266-1276.

Saling, M.M. (2009). Verbal memory in mesial temporal lobe epilepsy: Beyond material specificity. *Brain, 132,* 570–582.

Sawrie, S.M., Martin, R.C., Kuzniecky, R., et al. (1999). Subjective versus objective memory change after temporal lobe epilepsy surgery. *Neurology, 53,* 1511-1517.

Sheslow, D. & Adams, W. (2004). Wide Range Assessment of Memory and Learning – 2nd edition: Administration and technical manual. Lutz, Fl.: Psychological Assessment Resourses

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

Sinclair, D.B., Wheatley, M., Snyder, T., Gross, D., & Ahmed, N. (2005). *Pediatric Neurology, 32,* 257-263.

Smith, M.L., Elliot, I.M., & Lach, L. (2006). Memory outcome after pediatric epilepsy surgery: Objective and subjective perspectives. *Child Neuropsychology, 12*, 151-164.

Strauss, E., Hunter, M., & Wada, J. (1993). Wisconsin card sorting performance, effects of age of onset of damage and laterality of dysfunction. *Journal of Clinical and Experimental Neuropsychology, 15,* 896-902.

Stretton, J. & Thompson, P.J. (2012). Frontal lobe function in temporal lobe epilepsy. *Epilepsy Research*, *98,* 1 – 13.

Stuss, D.T. (2011). Functions of the frontal lobes: Relation to executive functions. *Journal of the International Neuropsychology Society, 17,* 759-765.

Swick, D. & Knight, R.T. (1999). Contributions of prefrontal cortex to recognition memory: Electrophysiological and behavioral evidence. *Neuropsychology, 13,* 155-170.

Szabo, C.A., Wyllie, E., Standford, L.D., Geckler, C., Kotagal, P., Comair, Y.G. & Thornton, A.E. (1998). Neuropsychological effect of temporal lobe resection in preadolescent children with epilepsy. *Epilepsia, 39* (8), 814-819.

Wang, W., Lioou, H., Chen, C., Chiu, M., Chen, T., Cheng, T., & Hua, M. (2011). Neuropsychological performance and seizure-related risk factors in patients with temporal lobe epilepsy: A retrospective cross-sectional study. *Epilepsy & Behavior, 22,* 728-734.

Wechsler, D. (2003). WISC-IV technical and interpretive manual. San Antonio, TX: Psychological Corp.

Wechsler, D. (1997). The Wechsler Adult Intelligence Scale - 3rd edition. San Antonio, TX: Psychological Corp.

Westerveld, M., Sass, K.J., Chelune, G.J., Hermann, B.P., Barr, W.B., Loring, D.W., et al. (2000). Temporal lobectomy in children: Cognitive outcome. *Journal of Neurosurgery, 92* (1), 24-30.

Wheless, J.W. & Kim, H.L. (2002). Adolescent seizures and epilepsy syndromes. *Epilepsia, 43(3),* 33-52.

Williams, J., Griebel, M.L., Sharp, G.B., & Boop., F.A. (1998). Cognition and behavior after temporal lobectomy in pediatric patients with intractable epilepsy. *Pediatric Neurology, 19* (3), 189-194.

Williams, J. & Sharp, G.B. (1999). Epilepsy in Yeates, K.O., Ris, M.D., & Taylor, H.G. (Eds.) *Pediatric Neuropsychology* (pp.47-73). New York: Guildford Press.

Wingenfeld, S.A., Lachar, D., Gruber, C.P., & Kline, R.B. (1998). Development of the teacher-informant student behavior survey. *Journal of Psychoeducational Assessment,* 16, 226.