11-29-2012 12:00 AM

Severity of Epilepsy and Parent-Perceived Cognitive Functioning in Children with New-Onset Epilepsy: A Prospective Study of Family Factors as Mediators and Moderators

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A thesis submitted in partial fulfillment of the requirements for the degree in Master of Science

SEVERITY OF EPILEPSY AND PARENT-PERCEIVED COGNITIVE FUNCTIONING IN CHILDREN WITH NEW-ONSET EPILEPSY: A PROSPECTIVE STUDY OF FAMILY FACTORS AS MEDIATORS AND MODERATORS

(Spine Title: Mediators and Moderators of Family Factors in Children with New-onset Epilepsy)

(Thesis format: Monograph)

by

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of the requirements for the degree of
Master of Science

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
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entitled:

Severity of epilepsy and parent-perceived cognitive functioning in children with new-onset epilepsy: a prospective study of family factors as mediators and moderators

is accepted in partial fulfillment of the
requirements for the degree of
Master of Science

Date

Chair of the Thesis Examination Board

Abstract

Children with epilepsy are at risk for cognitive impairments. In addition to severity of epilepsy, family factors have been cited as influencing cognition in children. The relationship between severity of epilepsy and parent-perceived cognitive functioning as well as moderating and mediating effects of family resources, demands and functioning were examined. Data came from the Health-related Quality of Life of Children with Epilepsy Study (HERQULES). Multiple linear regressions were conducted to assess the relationship between severity of epilepsy and cognition, and moderating effects, while generalized estimating equations assessed mediating effects. Severity of epilepsy and parent-perceived cognitive functioning were inversely related. Family resources acted as a significant moderator in this relationship. Neither family demands nor family functioning had a significant mediating effect, which may be due to the lack of variation in this sample. Further research should replicate the moderating results and indicate the importance of family factors in managing epilepsy.

Keywords: Severity of epilepsy, cognitive functioning, family, family resources, family demands, family functioning, paediatric or childhood epilepsy.

Acknowledgments

I would like to recognize the individuals who contributed to the successful completion of this thesis work and provided me with guidance and feedback throughout the process.

I would like to thank:

Dr. Kathy Speechley

Dr. Guangyong Zou

Dr. William Avison

Dr. Mark Ferro

I also want to acknowledge my partner, friends and family for their invaluable support throughout the past two years.

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List of Abbreviations

AEDs	Anti-Epileptic Drugs
APGAR	Family Adaptability, Partnership, Growth, Affection, and Resolve
BECTS	Benign Epilepsy with Centro-Temporal Spikes
CAE	Childhood Absence Epilepsy
CES-D	Centre for Epidemiological Studies Depression Scale
CVLT	California Verbal Learning Test
FCC	Family-Centred Care
FILE	Family Inventory of Life Events & Changes
FIRM	Family Inventory of Resources for Management
FLE	Frontal Lobe Epilepsy
FM	Family Mastery
FSIQ	Full Scale IQ
GASE	Global Assessment of Severity of Epilepsy
GEE	Generalized Estimating Equations
HERQULES	Health-Related Quality of Life in Children with Epilepsy study
HRQL	Health-Related Quality of Life
QOLCE	Quality of Life in Childhood Epilepsy
SAS	Statistical Analysis Software
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
TDM	Tailored Design Method
TLE	Temporal Lobe Epilepsy
TONI-II	Test of Non-Verbal Intelligence-II
WISC	Weschler Intelligence Scale for Children
WRAT	Wide Range Achievement Test

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Chapter 1 – Introduction and Research Objectives

1 Outline

This thesis examines the relationship between severity of epilepsy and parent-perceived cognitive functioning in children with new-onset epilepsy. Specifically, the study explores the role that family factors (demands, functioning and resources) may play in this association to improve understanding of the mechanisms behind cognitive outcomes in children with new-onset epilepsy. The ultimate goal of this study is to further clarify these relationships to provide insight into potential interventions that may improve the health-related quality of life in children with epilepsy.

1.1 Background

Epilepsy is a heterogeneous collection of neurological conditions and syndromes characterized by recurrent (two or more), unprovoked, paroxysmal seizures (Cowan, 2002; International League Against Epilepsy, 1993; Pellock, Dodson & Bourgeois, 2001). Seizures are the overt manifestation of an underlying brain abnormality occurring from multiple causes (Cowan, 2002). Approximately 55-75% of all epilepsy cases are of an unknown cause (Cowan, 2002).

It is estimated that worldwide, 10.5 million children under the age of 15 have active epilepsy (Guerrini, 2006). Population-based studies on childhood-onset epilepsy estimate that the annual incidence rates in developed countries ranges from 41 to 50 per 100,000 (Forsgren, 2004). In Canada, the prevalence of epilepsy in children 0 to 11 years of age is estimated to be 2.5 per 1,000 (95% CI: 2.1-3.0) and 4.4 (95% CI: 3.4-5.8) per 1,000 in children 12 to 14 years of age (Tellez-Zenteno, Pondal-Sordo, Matijevic & Wiebe, 2004). In the United States, approximately 150,000 children and adolescents will obtain medical attention for a newly occurring seizure disorder each year, making convulsive disorders (including epilepsy) one of the most common neurological problems in children (Hauser, 1994).

1.2 Brief Overview of Cognitive Functioning in Children with Epilepsy

Epilepsy is known to affect cognitive functioning in children (Jones, Siddarth, Gurbani, Shields & Caplan, 2010). Cognition can be characterized as the capacity of the brain to process information and to program adaptive behaviour. This includes the ability to solve problems, to memorize information, or to focus attention (van Rijckevorsel, 2006). When seizures occur, abnormal neuronal activity may have a significant impact on the normal cognitive processes of affected individuals (Motamedi & Meador, 2003).

Oostrom et al. (2003) compared the cognitive development of children with newly diagnosed epilepsy to healthy age- and sex-matched classmates and observed that children with epilepsy obtained lower scores in components of language and attention than control subjects (Oostrom et al., 2003). Children with a recent diagnosis of epilepsy also have demonstrated impairments on measures of intelligence, executive function, language and psychomotor speed (McCagh, Fisk & Baker, 2009). Although numerous studies indicate that cognitive functioning may be impaired in children with new-onset epilepsy, the prevalence of this impairment has not been estimated. This may in part be due to the lack of consensus regarding what should be considered "impaired" in the distribution of psychological test scores for cognitive functioning (Loring & Meador, 2009). Despite this, cognitive impairment is considered a core clinical feature of paediatric epilepsy (Loring et al., 2009).

More information is needed regarding the particular mechanisms whereby epilepsy affects cognitive functioning. There is some debate regarding which aspects of the disorder have the greatest effect on cognition (Vingerhoets, 2006). Some researchers have attempted to tease out the separate effects of clinical features such as seizure frequency, age at onset, anti-epileptic drugs (AED) and duration of active epilepsy. The results regarding the association between clinical aspects of epilepsy and cognitive functioning, which will be reviewed more thoroughly in Chapter Two, are inconsistent. To resolve the inconsistencies, additional research is necessary. There is evidence that the more severe the clinical aspects of epilepsy are (i.e., high seizure frequency, long duration of active epilepsy), the more cognitive functioning will be effected (Bjornaes,

Stabell, Henriksen & Loyning, 2001; Souza-Oliveira et al., 2010). This is why one particular clinical aspect of epilepsy, severity, is the focus here.

In an effort to better understand the mechanisms behind cognitive outcomes in children with new-onset epilepsy, this thesis investigates the association between severity of epilepsy and cognitive functioning and the role of family factors in this relationship.

1.3 The Importance of Researching Cognition in the First Years after Diagnosis

Several longitudinal studies evaluating associations between clinical aspects of epilepsy and cognitive functioning have focused on prevalence samples of children (Aldenkamp & Meinardi, 1992). As a result, it is difficult to know whether an observation of stable scores on cognitive functioning over time is due to the fact that these studies were conducted during a stable phase after the onset of epilepsy in prevalence samples, while the critical period might be the first years after diagnosis (Aldenkamp & Meinardi, 1992; Meinardi, Aldenkamp & Nunes, 1992). While some studies conclude that cognitive functioning deteriorates slowly over the course of epilepsy, this interpretation of the findings may be incorrect because of when testing took place. In studies that begin assessments at the onset of epilepsy, retests across time actually point to a process of deterioration in cognitive functioning beginning soon after diagnosis. Therefore, it is important to recognize that follow-up studies of cognitive functioning in epilepsy should continue to start as soon as possible after the onset of epilepsy to identify the true course of cognitive functioning (Neyens, Aldenkamp & Meinardi, 1999).

1.4 Implications of Cognitive Functioning Later in Life

The presence of even static cognitive impairments in childhood and adolescence may have long-term implications. Research in the general population has shown that lower childhood intelligence at 11 years of age is associated with a greater risk of adverse cognitive outcomes decades later, while higher childhood intelligence scores are associated with better cognitive outcomes (Hermann & Seidenberg, 2007). This developmental course of cognitive functioning can potentially predict the burden that may present later in life. This is why management of cognitive impairments is important

to take into account when treating a child with epilepsy at diagnosis. Children who show signs of cognitive impairment shortly following the time of diagnosis can provide compelling rationale for cognitive evaluation of all children newly diagnosed with epilepsy. This is a window of opportunity during which effective intervention may lessen the long-term cognitive burden of epilepsy (Loring et al., 2009).

1.5 The Importance of Family Factors in Childhood Epilepsy

In addition to the clinical aspects of chronic conditions, family factors play an important role in determining quality of life for children living with chronic illness. Family factors include: coping strategies, demands and stresses, interaction, resources, functioning, and support that influence children (Grey, Knafl & McCorkle, 2006; Hartz, Giefer & Rimm, 1977). Wallander, Varni, Babani, Banis and Wilcox (1989) reported that family resources are an important component for better psychological adjustment in children with chronic illnesses. A study evaluating adjustment in children with intractable epilepsy revealed that indicators of family functioning were second only to seizure frequency in predicting difficulties in adjustment (McCusker, Kennedy, Anderson, Hicks & Hanrahan, 2002).

Family factors have been cited recently as influencing cognitive functioning in children with epilepsy (Jones et al., 2010) but little research has been done in this area. Oostrom et al. (2003) found that having parents who were thrown off balance in the time following the diagnosis and who failed to continue their regular parenting habits was associated with poorer cognitive and behavioural functioning in children with epilepsy. It is important to investigate this further to potentially address problems that may occur in the family early as a way to reduce behavioural and cognitive problems. With effective interventions in place, family factors may change in a more positive direction following diagnosis and minimize negative outcomes in children with epilepsy (McCusker et al., 2002).

1.6 Research Objectives

This thesis has two objectives:

1. To assess the relationship between severity of epilepsy at six months after diagnosis and parent-perceived cognitive functioning two years after diagnosis in children with new-onset epilepsy.

It is hypothesized that there will be an inverse relationship between severity of epilepsy and cognitive functioning. In cases of more severe epilepsy, cognitive function will be lower.

2. To assess the role of three family factors one year after diagnosis in the relationship between severity of epilepsy and parent-perceived cognitive functioning in children with new-onset epilepsy:

It is hypothesized that:

(a) Family resources will moderate the effects of disease severity on cognitive functioning in children with new-onset epilepsy, such that for those with more family resources, severity of epilepsy will have a less negative effect on cognitive functioning;

(b) Family demands will mediate the relationship between severity of epilepsy and cognitive functioning. That is, in cases of more severe epilepsy, families will endure more demands and this will result in poorer cognitive outcomes;

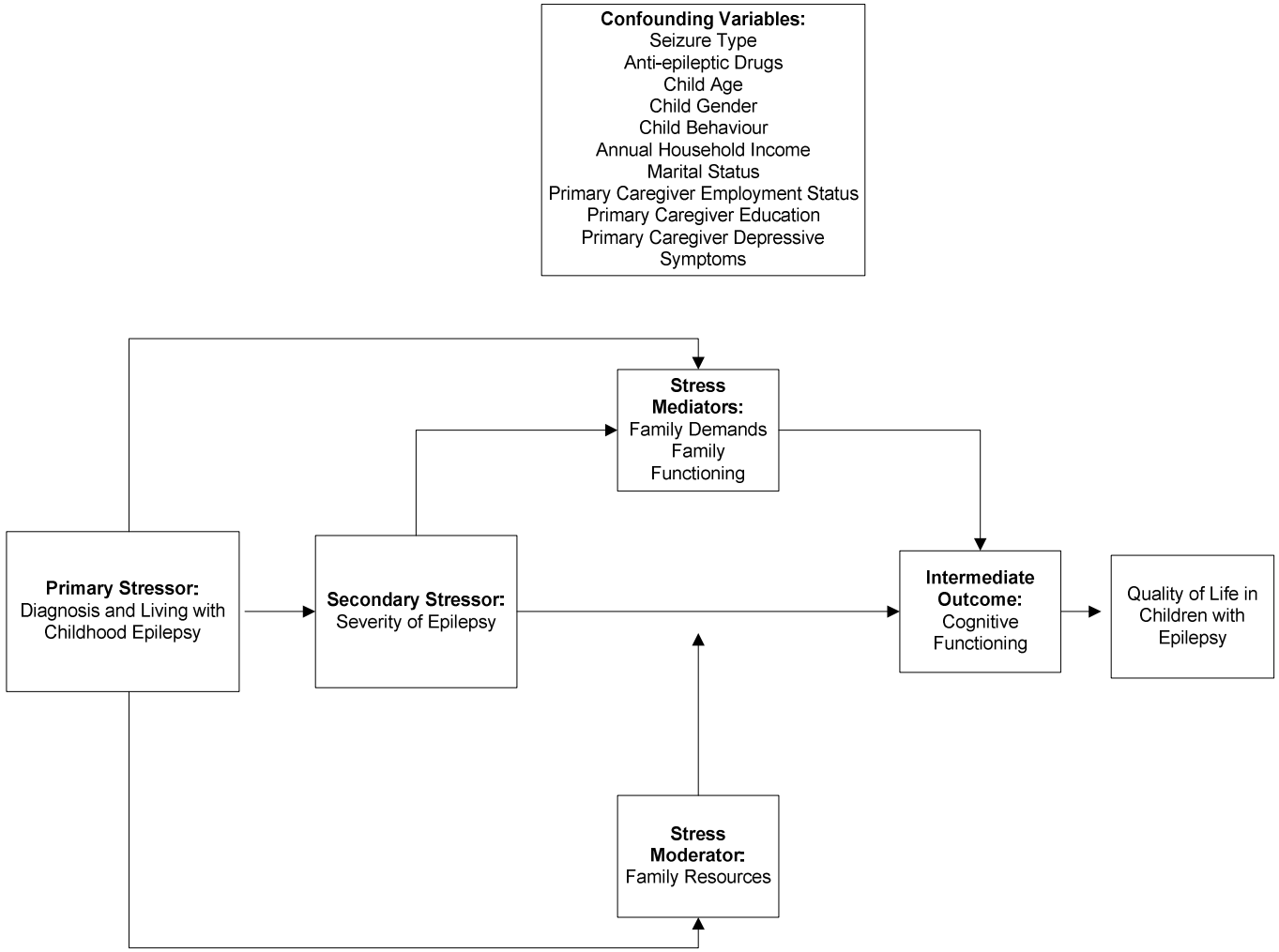
(c) Family functioning will mediate the relationship between severity of epilepsy and cognitive functioning. That is, in cases of more severe epilepsy, families will experience poorer family functioning, and this will result in poorer cognitive outcomes.

1.7 Conceptual Framework

The conceptual framework used to guide this thesis was the Stress Process Model that was adapted by Pearlin, Lieberman, Menaghan and Mullan (1981), as shown in Figure 1. Pearlin et al. (1981) developed a stress process paradigm using social stress theory to examine the ways in which stressors and psychosocial resources mediate and moderate the association between social structure and an array of health outcomes (Turner & Lloyd, 1999). This framework makes it possible for researchers to identify potential targets for intervention to minimize or eliminate the negative effects stressors may have on one's health. The stress process model classifies stressors as primary and secondary, referring to the temporal order in which stressors occur. The model presumes that stressors do not arise concurrently, but appear consecutively as the process unfolds, which clarifies the order between exposure and outcome. In this thesis, the role of family factors as stress mediators and moderators will be assessed. Stress mediators are defined as variables on a pathway that connect the exposure to stress to its manifestations (Avison & Thomas, 2010). For example, the diagnosis of epilepsy and its severity may result in increased family demands, and in turn these demands can lead to less attention to the child's development and affect cognitive functioning. Stress moderators can be seen as variables that can buffer the effect of exposure on outcome (Avison & Thomas, 2010). For example, the effect of severity of epilepsy on cognitive functioning may increase or decrease dependent on the level of family resources.

Applying the stress process to the study of childhood epilepsy, the impact of the diagnosis of epilepsy and learning to live with childhood epilepsy can be viewed as primary stressors, and the severity of the child's epilepsy as a secondary stressor. Potential stress mediators are family demands and family functioning and a potential stress moderator is family resources. In this thesis research, parent-perceived cognitive functioning is an intermediate outcome and health related quality of life (HRQL), the overall outcome. The model also depicts a number of potential confounding variables that may influence the process.

Figure 1. Conceptual Framework Based on a Stress Process Model used to Guide Research in Childhood Epilepsy



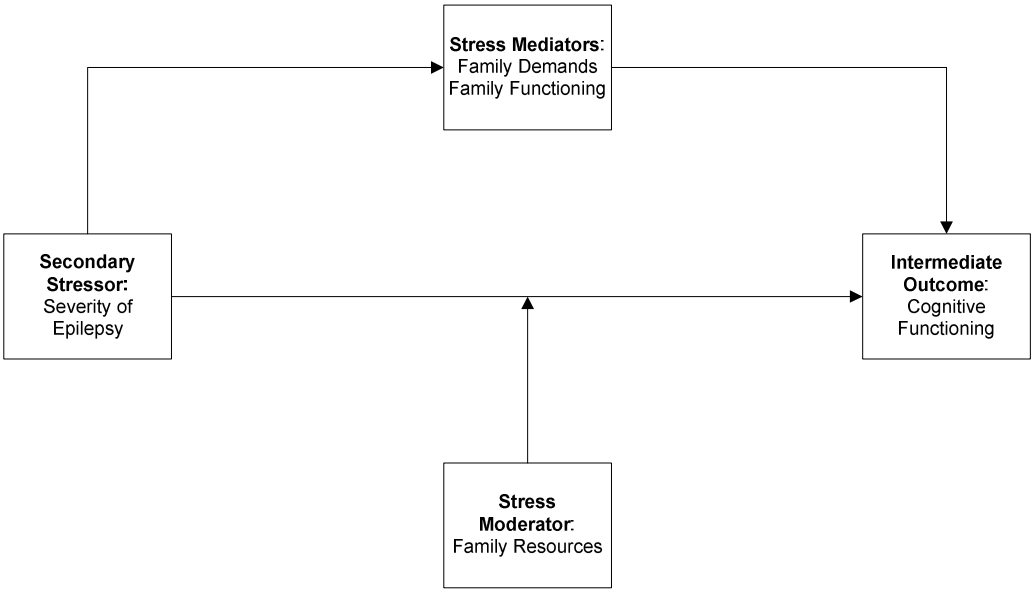
The most frequently studied stressors exist in two forms: life events and chronic strains. Life events refer to stressors that occur at a distinct and identifiable point in time (e.g., the diagnosis of childhood epilepsy). Chronic strains are stressors that are persistent and likely to last over time (e.g., living with epilepsy). Pearlin et al. (1981) state that life events and chronic strains potentially produce stress in two ways: (1) life events lead to stress by adversely altering the meaning of persistent life strains; (2) life events may create new strains or intensify preexisting strains and, in turn, perpetuate stress. Role overload can be experienced by caregivers and is defined as a condition that exists when demands on energy and stamina exceed the individual's capacities (Pearlin, 1989). Role overload is common among those taking care of chronically ill relatives. This is an important factor for this thesis as the primary caregivers are affected first hand by the child's epilepsy. Primary caregivers may also experience interpersonal conflicts within set roles, which is a type of chronic strain that is reported often (Pearlin, 1989). This type of strain often arises among those who regularly interact with each other, such as in wife-husband and parent-child relationships (Pearlin, 1989).

Evidence suggests that family factors can exert mediating and moderating effects on the relationship between stressors and health outcomes. Elgar, Mills, McGrath, Waschbusch and Brownridge (2007) showed that the quality of the child's family environment mediated the impact of maternal depressive symptoms on child and adolescent maladjustment over a two-year period. Baum et al. (2007) reported that family resources moderated the relationship between temperament and internalizing and externalizing behavioural problems in children with epilepsy. Lastly, Ferro, Avison, Campbell and Speechley (2011) found that family resources moderated the association between maternal depressive symptoms and children's health related quality of life (HRQL) during the 24 months after diagnosis of epilepsy.

To our knowledge, no one has examined the role that family factors play in the relationship between severity of epilepsy and cognitive functioning in children

with new-onset epilepsy. The theoretical foundation of the stress process model, taken together with empirical evidence from other areas of research, support the hypothesis that family factors may be part of the pathway between severity of epilepsy and cognitive functioning. Family resources may act as a stress moderator between this relationship of interest. Also, family demands and family functioning as stress mediators represent components along the causal pathway, that if significant, may be amenable to interventions to alleviate the potential negative influence that epilepsy severity may have on cognitive functioning in children. The specific segment of the stress process model that is explored in this thesis is presented in Figure 2.

Figure 2. Segment of the Stress Process Model Explored in this Thesis



Chapter 2 – Literature Review

2 Chapter Overview

This chapter begins by defining some key concepts. The main goal of the chapter is to review five separate bodies of literature relevant to this thesis as outlined in the conceptual model presented in Figure 1. The strategy used to search the literature is described in Appendix A. Section 2.2 reviews the relationship between the secondary stressor, severity of epilepsy, and cognitive functioning in children with epilepsy. Section 2.3 reviews the relationship between seizure type and cognitive functioning in children with epilepsy. Section 2.4 explains the impact of epilepsy on the family. Section 2.5 reviews the association between the stress mediators and moderators on cognitive functioning. The last section (2.6) addresses limitations of prior research from which objectives of this thesis emerge.

2.1 Definitions

It is important to define both the exposure (severity of epilepsy) and outcome (cognitive functioning) before proceeding.

Severity of epilepsy captures many of the important aspects that comprise the clinical condition: seizure frequency and severity, extent of seizure control, duration of active epilepsy and treatment with anti-epileptic drugs (Speechley et al., 2008). This is distinct from severity of seizures, which focuses exclusively on the seizures themselves and does not incorporate any other aspects of epilepsy. In an effort to provide a more complete clinical representation of the severity of the patient's condition, this thesis focuses on the more comprehensive construct of severity of epilepsy.

The terms cognitive functioning and cognitive impairment are often used interchangeably in reference to the health outcome in this thesis. Cognitive functioning refers to the whole range of cognition. As outlined in Chapter One, cognition is the brain's capacity to process information accurately and to program adaptive behaviour, involving the ability to solve problems, memorize

information, or focus attention (Rijckevorsel, 2006). Cognitive impairment refers specifically to the lower end of the range of cognition, below that considered to be normal.

There is also some confusion around distinguishing between the terms, "cognitive functioning" and "intelligence" in the literature. Intelligence scales, such as the Weschler Intelligence Scale for Children (WISC) (Weschler, 2004), are used to measure cognitive functioning. Although there is considerable variability in cognitive functioning among those diagnosed with epilepsy, it should be noted that epilepsy patients usually have a normal distribution of intelligence scores. Thus it is important to not simply classify children with epilepsy as having normal or below normal intelligence, but also recognize that there will be children with normal intelligence whose cognitive functioning can still disadvantage them. Accordingly, it is better to use a continuous measure allowing the opportunity to capture the full range of cognitive functioning including variation across specific domains rather than a dichotomy that classifies children as having normal or abnormal test scores.

The definition of intelligence has been debated for decades, and there remains a lack of consensus (Wang, 1995). However, the definition deemed most appropriate for this thesis was the one offered by David Wechsler (1975) viewing intelligence as an individual's ability to adapt and constructively solve problems in the environment. As this definition suggests, Wechsler viewed intelligence in terms of performance and not capacity. It may not be appropriate to assume that cognition and intelligence represent the same concept. Since IQ-tests were not designed to investigate brain-behaviour relationships, these measures may underestimate changes in a broader range of cognitive functions (Vingerhoets, 2006). Measures of intelligence were devised to predict how well children would do in a school setting and not to identify difficulties in brain function (Dodrill, 2004). That is why validated neuropsychological tests can clearly evaluate a broader range of functioning than measures of intelligence (Dodrill, 2004).

The Wechsler Intelligence Scale for Children (Wechsler, 2004) appears to be the most commonly used measure of cognitive functioning in paediatric studies. Over the years, the WISC has been adapted with several additions, such that intelligence is now widely viewed as having a hierarchical structure with more specific abilities comprising several broad cognitive domains (Wechsler, 2003a). Finally, Wechsler avoided defining intelligence in purely cognitive terms because he believed that other attributes, such as planning and goal awareness, enthusiasm, field dependence and independence, impulsiveness, anxiety, and persistence all contributed to intelligent behaviour (Wechsler, 2003a). This can be deemed problematic because this test is consistently used to measure cognitive abilities. These notable issues suggest that the most recent version, the WISC-IV should be viewed as mixed ability tests (Beal, 2004). It is important for researchers to acknowledge that children may have underlying cognitive problems yet still have intelligence scores within the normal range.

2.2 Severity of Epilepsy and Cognitive Functioning

Several studies have assessed the association between severity of epilepsy and cognitive functioning in children with epilepsy. The following clinical aspects of childhood epilepsy have been reported as associated with impaired cognitive functioning: uncontrollable seizures, high seizure frequency, long duration of seizures, symptomatic aetiology, early onset of epilepsy, structural cerebral damage caused by prolonged or repetitive seizures and treatment related factors (Hoie et al., 2005; Meador, 2002). The vast majority of research indicates that severity of epilepsy is related to cognitive functioning.

In the subsections below, frequency, seizure control and duration are discussed separately because the majority of studies looking at clinical aspects of epilepsy and cognitive functioning attempt to look at these effects separately. In reality, the independent effects of seizure duration, as independent from seizure frequency or lack of seizure control are difficult to isolate, but it is important to recognize and attempt to tease out the individual effects of each factor.

2.2.1 Frequency of Seizures

Frequent seizures have often been associated with the deterioration of cognitive processes in children with epilepsy. Aldenkamp (1997) describes the biological processes taking place, stating that frequent seizures can interfere with brain development and have a long-term impact on cognition through the inhibition of mitotic cell activity, which affects myelinization thus reducing cell numbers and cell size. Evidence suggests that high seizure frequency and duration among those with temporal lobe epilepsy are associated with more severe hippocampal atrophy and cognitive impairment. Researchers believe that perhaps this may be through secondary neuronal metabolic and structural deterioration (Motamedi et al., 2003). Repeated magnetic resonance imaging showed progressive hippocampal reduction following frequent seizures in several case-studies (Vingerhoets, 2006). Imaging also showed an association between seizure frequency and hippocampal volume loss in prospective cohort studies, although across studies this is not always confirmed (Vingerhoets, 2006).

In a prospective cohort study, 169 patients with both generalized and partial epilepsy were observed to evaluate the relationship between severity of epilepsy and cognitive functioning. It was found that seizures occurring as frequently as one or more times daily were associated with significantly lower full-scale IQ (FSIQ) scores measured by the WISC-III ($p<0.001$; Nolan et al., 2003). Another prospective cohort study involving 34 patients (17 of whom were children) assessed at 3.5 and 6.0 years after the study began found that frequent seizures in childhood focal epilepsies represented a considerable risk for decreased intellectual functioning over this period as measured by the WISC ($p<0.05$; Bjornaes et al., 2001). This deterioration was found in the children but not the adults studied (Bjornaes et al., 2001). In a prospective non-randomized open clinical trial, 28 children with generalized and partial epilepsy were assessed. Aldenkamp and Arends (2004) found that frequent seizures were associated with impairment of alertness/mental slowing in children ($F=2.539$; $p<0.02$), but not associated with FSIQ ($F=0.431$; $p=0.05$).

Lack of Seizure Control. In this thesis, lack of seizure control is discussed within the context of seizure frequency. This is because frequent seizures can be due to lack of seizure control. In the absence of a cure for epilepsy, the goal of the management of childhood epilepsy is to reduce or control seizures with anti-epileptic medications (Pellock & Appleton, 1999).

Lack of seizure control can cause long-term negative effects for children with epilepsy. Specifically, children whose seizures were not controlled showed greater cognitive deterioration (Tamer, 1999). Explaining the effect of lack of seizure control and cognitive functioning in biological terms, Souza-Oliveira et al. (2010) reported that recurrent seizures can modify a wide range of cerebral processes during development that are essential for the correct formation and functioning of brain circuits. Therefore, patients with intractable epilepsy have more diffuse and severe cognitive impairments than patients with good seizure control (Souza-Oliveira et al., 2010).

Specifically, it was found that seizure control by medication can improve performance on the following subtests: Vocabulary (p=0.04), Arithmetic (p=0.002), Comprehension (p=0.002), Picture Completion (p=0.02), Digit Span (p=0.002), Picture Arrangement (p=0.009) and Block Design (p=0.01) when compared to those without medication control (Souza-Oliveira et al., 2010). Another prospective cohort study assessed 69 children with epilepsy and 66 healthy controls to examine the effect of epilepsy variables on cognitive functioning. Analyses revealed that children who had a six-month seizure remission after one year could not be distinguished from the control group on cognitive functioning (μ difference 0.52, 95% CI: 0.11, 0.94) (Schouten et al., 2002). Moreover, higher IQ was observed in children with good seizure control (Farewell, Dodrill & Batzel, 1985).

In another prospective cohort study, 72 children with epilepsy underwent cognitive evaluations within two weeks of initial diagnosis and yearly thereafter for an average of 4 years (Bourgeois, Prensky, Palkes, Talent & Busch, 1983). While no statistically significant changes in IQ were detected, 8 of the 72 (11.1%) patients with epilepsy had a persistent decrease in IQ of 10 points or more across time

points, which is clinically relevant. These patients had epilepsy that was more difficult to control ($p<0.005$), and their seizures began at an earlier age ($p<0.05$).

Lastly, Sogawa, Masur, O'Dell, Moshe and Shinnar (2010) conducted a prospective cohort study that followed a sample of 258 patients after their first unprovoked seizure, for a median of 15 years. At the time of follow-up, >50% of children had standardized cognitive testing. Of the 163 children who completed cognitive testing, children with a single seizure tended to score higher than children with epilepsy on the measures of the Wide Range Achievement Test (WRAT) ($p=0.08$), Test of Non-Verbal Intelligence-II (TONI-II) ($p=0.02$) and Weschler Intelligence Scale for Children (WISC) ($p=0.07$). There was no significant difference between children with a single seizure and sibling controls. However, a recent study reported that even single seizures can lead to a temporary change in cognitive performance but persists over time only when the seizure frequency is high or postictal effects are prolonged (Tromp et al., 2003).

Evidence presented above largely supports that lack of seizure control, specifically frequent seizures that are uncontrolled, are associated with decreased cognitive functioning in children with epilepsy. For the majority of seizure types, there is evidence that cognitive impairment arising from seizure activity can be reduced by effective seizure control. Effective seizure control is especially relevant to children with epilepsy, where the negative impact of seizures on cognitive functioning may accumulate over time (McCagh et al., 2009). It is concluded that recurrent seizures may represent a considerable risk for cognitive decline in children, but not in adults due to the different stages in the development of intellectual abilities (Bjornaes et al., 1999).

2.2.2 Duration of Active Epilepsy

Investigations of the effects associated with duration of active epilepsy have produced similar results. Duration of active epilepsy is distinct from age of onset, as it describes how long a child has had active seizures throughout his/her disease course, but studies often analyze age of onset and duration of active epilepsy together. Generally, the effect of the disease's duration is difficult to separate from

that of age of onset (Carreno, Donaire & Sanchez-Carpintero, 2008). Little research has examined the effect of duration of active epilepsy on cognitive functioning.

Nolan et al. (2003) explained that duration of active epilepsy had a significant but low correlation with full scale IQ (FSIQ; r=0.17, p=0.025). When age of onset was considered, duration of active epilepsy did not have an independent effect on FSIQ (combined r=0.42, R^2=0.17, p<0.001) and no longer made a significant contribution (p=0.27). Similar results were found in a case-control study observing 57 children with complex partial seizures and 27 sibling controls (Schoenfeld et al., 1999). Both earlier age at onset (p<0.01) and increased percentage of lifetime with active epilepsy (p<0.05) were associated with greater impairment on the summary measure of overall cognitive performance. However, a stepwise regression analysis confirmed that age at seizure onset was the only clinical seizure variable to emerge as a significant predictor of cognitive functioning (Schoenfeld et al., 1999).

In summary, the few studies above illustrate the relationship between duration of active epilepsy and cognitive functioning. Observational studies have shown that duration of active epilepsy is associated with cognitive functioning when other clinical aspects of epilepsy are not present.

2.3 Seizure Type and Cognitive Functioning

The diagnosis of epilepsy includes a classification of a seizure type. There are multiple types of seizures with differential effects on cognitive functioning due to the part of the brain that is active during an epileptic seizure. It is important to consider these specific effects on cognitive processes and to note that a patient can be diagnosed with more than one seizure type. Since multiple seizure types can be diagnosed in one patient, it is assumed that the classifications represent the predominant seizure type. However, some patients have seizure types that remain unclassified, making it difficult to individually examine each seizure type separately.

Seizures fall into two main categories: Partial (focal) or Generalized (Banerjee et al., 2009). Partial seizures are characterized by seizures that occur in a local area of the brain. Partial seizure types are then subdivided into simple partial seizures (no alteration in consciousness) and complex partial (alteration of consciousness). Benign childhood epilepsy is also characterized by partial seizures. On the other hand, generalized seizures involve the entire brain simultaneously. Generalized seizure type includes absence, tonic-clonic and myoclonic seizures. Epilepsy characterized by generalized seizures may also be categorized as partial with secondary generalization. This is if a clinical description of an antecedent symptom (aura), or clear EEG signature of focality is indicated.

In the majority of population-based prevalence studies, partial seizures are most prevalent with estimates at approximately 60% and generalized seizures at around 40% (Berg, Levy, Testa & Shinnar, 1999; Berg, Shinnar, Levy & Testa, 1999; Silinpaa, Jalava & Shinnar, 1999).

It is estimated that of focal seizures such as those characterized by temporal lobe epilepsy (TLE) and frontal lobe epilepsy (FLE), it is estimated that simple partial seizures comprise from 6 to 12%, complex partial seizures from 8 to 31%, and partial seizures with secondary generalization from 7 to 29% (Cowan, Bodensteiner, Leviton & Doherty, 1989; Eriksson and Koivikko, 1997; Kramer et al., 1998; Murphy, Trevathan & Yeargin-Allsopp, 1995; Sidenvall, Forsgren & Heijbel, 1996; Waaler, Blom, Skeidsvoll & Mykletun, 2000). Benign childhood epilepsy with centrotemporal spikes, also known as benign rolandic epilepsy, represents 8 to 23% of childhood epilepsies (ILAE, 1989). In terms of generalized seizures, absence seizure comprise from 2 to 16%, tonic-clonic seizures from 12 to 27%, and myoclonic seizures from 1 to 9% (Cowan et al., 1989; Eriksson and Koivikko, 1997; Kramer et al., 1998; Murphy et al., 1995; Sidenvall et al., 1996; Waaler et al., 2000).

The seizure types reviewed below are the most common in children diagnosed with epilepsy and are ordered based on their reported prevalence in the paediatric population.

2.3.1 Simple/Complex Partial Seizures

Both children with Temporal Lobe Epilepsy (TLE) and Frontal Lobe Epilepsy (FLE) are at risk for cognitive impairments. Using magnetic resonance volumetric imaging, Hermann, Seidenberg & Bell (2002) documented generalized brain volume loss and an associated decline in performance in intellectual (measured by the age appropriate Weschler Intelligence Scale) and memory measures (verbal and non-verbal selective reminding test) in childhood temporal lobe epilepsy. In this case-control study, the sample included 53 patients with temporal lobe epilepsy (37 early age at onset vs. 16 late age onset) and 62 healthy controls. Patients with early age onset epilepsy exhibited poorer cognitive performance than those with late onset epilepsy ($p \leq 0.04$ on 7 of 12 measures) and 62 healthy controls ($p \leq 0.002$ on all measures) (Hermann et al, 2002).

In a cross-sectional study, Cormack et al. (2007) assessed 79 patients with TLE. Intellectual dysfunction (defined as IQ <79 measured by age appropriate Weschler Intelligence scale) was present in 57% of all cases of unilateral temporal lobe epilepsy indicating 'low' or 'exceptionally low' cognitive functioning. In another cross-sectional study of 43 children with TLE, facial recognition was poorer in right compared to left TLE ($p=0.03$) and memory impairment was frequent in participants with both right and left TLE but there were no differences between the two groups on any memory measure (Gonzalez, Anderson, Wood, Mitchell & Harvey, 2007).

Frontal lobe epilepsy is the second most common type of partial epilepsy in children. Cognitive functioning in these children is similar to that of adults with FLE (Boone et al., 1988; Grattan & Eslinger, 1991). In a review of studies on FLE, Patrikelis, Angelakis and Gatzonis (2009) found that there are some common patterns in both adults and children. Both children and adults with FLE both show deficits in attention, response inhibition, psychomotor speed, motor programming, and planning, and they both manifest postsurgical impairments in verbal fluency when operated in the dominant hemisphere (Patrikelis et al., 2009). Moreover, compared to those with temporal lobe epilepsy (TLE), both children and adults

with FLE have fewer memory problems, but more attention and response inhibition problems (Patrikelis et al., 2009).

In a small cross sectional study of 18 patients (8 with FLE and 10 with TLE), Auclair, Jambaque, Dulac, LaBerge and Sieroff (2005) reported a deficit in preparatory attention in children with FLE ($p<0.05$). These results indicate that FLE affects the capacity of children to resist the interference of distracters, and that this deficit in preparatory attention is related to frontal lobe dysfunction in children with epilepsy. Hernandez et al. (2003) compared 16 pediatric patients with FLE to 8 patients with TLE and generalized absence epilepsy. The sample in this cross-sectional study was measured on a broad set of cognitive tests. Children with FLE were more impaired on tasks involving motor coordination ($p<0.05$) and planning abilities ($p<0.05$) than children with TLE or generalized absence epilepsy.

In summary, the literature indicates that temporal lobe epilepsy and frontal lobe epilepsy are associated with a decline in specific domains in cognition such as memory and attention.

Benign Rolandic Epilepsy. The nature of cognitive deficits reported in benign rolandic epilepsy has been inconsistent (Northcott et al., 2005). Although benign rolandic epilepsy usually occurs in children who are cognitively "normal", a variety of cognitive problems have been identified in those with active epilepsy. Verbal (Baglietto et al., 2001; D'Alessandro et al., 1990; Massa et al., 2001), visuomotor (D'Alessandro et al., 1990), nonverbal (Baglietto et al., 2001; Massa et al., 2001; Stephani, 2001), attention (Massa et al., 2001; Piccirilli et al., 1994; Weglage, Demsky, Pietsch & Kurlemann, 1997), language (Staden, Isaacs, Boyd, Brandi & Neville, 1998), executive functioning (Croona, Kihlgren, Lundberg, Eeg-Olofsson & Eeg-Olofsson, 1999; D'Alessandro et al., 1990; Lindgren et al., 2004), and memory deficits (Croona et al., 1999; Massa et al., 2001) have been reported.

Northcott et al. (2005) conducted a cross-sectional study of 42 patients with benign rolandic epilepsy. It was found that mean scores on cognitive tests of the epilepsy group were significantly different from normative means. Researchers found differences showing higher than expected means on measures of intellectual ability

and general language, but lower scores of memory and phonological awareness in children with benign rolandic epilepsy (range from $p<0.0005$ to $p=0.034$) (Northcott et al., 2005). A case-control study (Fonseca et al., 2007) found that 31 out of 42 children with benign epilepsy with centro-temporal spikes (BECTS) performed average or above average on the cognitive measure, Raven progressive matrixes. Another case-control study by Gunduz, Demirbilek and Korkmaz (1999) assessing 20 patients with benign rolandic epilepsy and 15 controls noted more difficulties in attention and response testing ($p<0.001$), language ($p=0.05$), and minor motor skills ($p<0.05$) compared to controls.

In a prospective cohort study involving 9 children, Baglietto et al. (2001) documented poorer performance on tests of visuospatial short-term memory ($p<0.001$), attention ($p<0.001$), cognitive flexibility ($p<0.01$), picture naming ($p<0.01$), verbal fluency ($p<0.001$), and visuoperceptual and visuomotor coordination ($p<0.0001$) in 9 children with benign epilepsy with centrotemporal or rolandic spikes compared to 9 controls. In a longitudinal study conducted by Deonna et al (2000), twenty-two children with benign rolandic epilepsy had cognitive testing. All but one child had normal IQ (>80). However, four had delayed language development and needed school support, two children had difficulties with short-term visuospatial memory and five with long-term memory (Deonna et al., 2000).

To summarize the literature on benign rolandic epilepsy, studies usually consist of small samples and epilepsy varying in severity. Benign rolandic epilepsy, when active in a child, has shown to be associated with deterioration in multiple areas of cognitive functioning. However, when seizures are controlled, there is a good prognosis.

2.3.2 Generalized Seizures

Considerable research has examined the relationship between generalized seizures and cognitive functioning in children. Children with generalized seizures have been reported to have good social adjustment but some patients have been reported to have behavioural and cognitive impairments (Guerrini, 2006).

Cross-sectional studies on small samples of patients with childhood absence epilepsy (CAE) have demonstrated that shortly after diagnosis, these children have cognitive (Henkin et al., 2005; Mandelbaum & Burack, 1997; Pavone & Niedermeyer, 2000; Williams et al., 1996) and linguistic problems (Caplan et al., 2001, 2002; Henkin et al., 2005). The cognitive impairments of children with CAE involve visual sustained attention (Levav et al., 2002), visual spatial skills (Pavone et al., 2001), verbal and non-verbal attention (Henkin et al., 2005), as well as verbal (Henkin et al., 2005; Hoie, Mykletun, Waaler, Skeidsvoll & Sommerfelt, 2006; Nolan et al., 2004), and nonverbal memory (Pavone et al., 2001). Similar results have been found in patients with short non-convulsive seizures who also experience impaired alertness and information processing speed (Aldenkamp & Arends, 2004).

In a cross-sectional study examining 57 children with various seizure types, those with generalized seizures demonstrated lower verbal intelligence scores than those with focal seizures (p=0.012), and children with generalized absence seizures performed significantly worse than those with focal seizures on a measure of short-term auditory memory (p=0.019; Bhise, Burack & Mandelbaum, 2009). Those with focal seizures secondarily generalized did not differ significantly on the vocabulary measure from those with focal seizures not secondarily generalized. Both focal groups with and without generalization scored significantly better than the primary generalized group on the vocabulary measure (secondarily generalized greater than primary generalized, p=0.029; non-generalized greater than primary generalized, p=0.054; non-generalized equal to secondarily generalized, p=0.812; Bhise et al., 2009). Children with secondarily generalized focal seizures had significantly better response time scores than both the non-generalized group (p=0.014) and the primary generalized seizure group (p=0.006; Bhise et al., 2009).

In a prospective cohort study of 43 children with new-onset idiopathic seizures, where the relationship between seizure type and cognitive functioning was assessed, Mandelbaum and Burack (1997) found at baseline, simple partial (μ=110.07), complex partial (μ=102.18), generalized convulsive (tonic-clonic) (μ= 104.39) and generalized non-convulsive (absence) (μ=99.53) were not statistically different (F=2.03, p=0.13). When the complex partial group was eliminated from

analysis, patients with generalized non-convulsive seizures were found to perform more poorly on cognitive measures than simple partial or generalized convulsive seizures ($F=4.25$, $p=0.05$). At a 6-month follow-up, there were no statistically significant differences among the four seizure types on the cognitive scores ($F=1.15$, $p=0.29$).

Henkin et al. (2005) examined 24 children with absence and generalized tonic-clonic seizures and 20 healthy controls in a case-control study. Children with both types of seizures had significantly lower performance then controls on several domains of cognitive functioning (Henkin et al., 2005). Specifically, in the verbal and non-verbal attention tests, the group with epilepsy performed significantly worse than the control group ($F[1,43]=8.3$, $p=0.006$, $F[1,43]=14.3$, $p=0.0005$ respectively) on the California Verbal Learning Test measure (CVLT; Henkin et al., 2005). The performance of the idiopathic generalized epilepsy group was significantly poorer than that of the control group in all subscales of the test. Further analysis revealed that the performance of the absence seizures group was significantly poorer than the control group on all subscales of the CVLT, excluding CVLT trial 5 (recognition memory; Henkin et al., 2005). The performance of the generalized tonic-clonic seizure group was poorer than that of the control group in all subscales; but, statistically significant differences were evident only in the CVLT trial 3 (attention) and immediate cued recall subscales (Henkin et al., 2005). In both subtests of the word fluency test (categorical, $p<0.05$; and phonological, $p\leq0.01$) the performance of the idiopathic generalized epilepsy group was significantly poorer than the control group (Henkin et al., 2005). The comparison between the control and study groups (absence and generalized tonic-clonic seizures) revealed that in the categorical fluency subtest, only the performance of the absence seizures group was significantly lower than that of the control group ($p<0.05$; Henkin et al., 2005). No significant difference was found among groups in the phonological fluency subtest (Henkin et al., 2005). Lastly, Bhise et al. (2009) found that children with absence seizures performed significantly worse than the focal group on a measure of short-term auditory memory ($p=0.019$).

To summarize, it is a commonality that previous studies usually involved small sample sizes with a variety of measures for cognitive functioning. Results from these studies identified that children with absence seizures perform more poorly on cognitive tests compared to those with focal seizures, generalized convulsive seizures and controls.

2.4 Impact of Epilepsy on the Family

When a member of the family has a serious illness, the family is confronted with the possibility of making major changes in their usual routine to accommodate illness demands. They are also challenged by the possibility of an altered future. The impact of epilepsy on the family is reviewed below.

2.4.1 Impact of Diagnosis and Course of Epilepsy on the Family

The diagnosis of a chronic illness in a child is an uncertain time for families (Knafl & Gilliss, 2002). In a study evaluating critical events for families whose children have chronic illnesses, 70% of parents stated that the time around diagnosis was the hardest time over the course of the illness (Clements, Copeland & Loftus, 1990). This may be related to the unpredictability and burden the family will face over the progression of the illness. Childhood epilepsy presents a series of consequences for the family (Ellis, Upton & Thompson, 2000).

There is considerable variability across conditions in children with regard to predictability of the illness course. Conditions that are characterized by an uncertain trajectory impose greater psychosocial demands on the family (Grey et al., 2006). Depending on the severity of the child's condition, uncertainty may produce a large burden on family relationships and life in general. Young children are completely dependent on their families for care of their chronic illness, and this dependency changes over time (Grey et al., 2006). This is the case for a chronic illness such as epilepsy. In epilepsy, the increased burden of care is related to: the extra needs of the child, finding and accessing medical and education services, and uncertainty of the future (Hobbs, Perrin & Ireys, 1985; Patterson, 1988; Patterson & Blum, 1996). Parents of children with chronic epilepsy may be stressed by substantial caretaking demands, the relative unpredictability of seizures themselves,

and the costs of medical care, including hospitalizations, medications, lost days at work and observation of adverse effects of the epilepsy and anti-epileptic medications on the child's cognitive, educational, and/or psychological growth (Mu, 2005; Ellis et al., 2000).

The fatigue and disease uncertainty that parents face combined with the need to provide daily medical management regimens are likely to affect many aspects of daily life (Barlow & Ellhard, 2006; Melnyk, Alpert-Gillis, Hensel, Cable-Beiling & Rubenstein, 1997). They often worry and express feelings of fear and incompetence as they manage their child's epilepsy by monitoring and recording seizures, adjusting medications, and supervising the safety of their child (Melnyk et al., 1997). The feeling of helplessness may be the results of parents not being able to control the seizures, which leads to a reduction in parental confidence and role certainty, which leads to an increase in stress (Melnyk et al., 1997). It has been documented that the constant adjustment to the needs of a sick child make it hard for parents to correctly judge the child's development capabilities (Sein, 2001). This difficulty in day-to-day living results in lower expectations for the child with epilepsy (Ellis et al., 2000).

Family factors that have been reported to affect families due to epilepsy are: family stress, marital difficulties, restriction to social life and low self-esteem of primary caregivers (McCagh et al., 2009). In a case-control study, 30 parents of children with new-onset epilepsy and 29 parents of healthy controls were compared on measures of parenting stress and activity patterns (Modi, 2009). A higher percentage of parents with a child with new-onset epilepsy experienced elevated life stress scores compared with parents of controls ($p<0.05$) (Modi, 2009). A post-hoc examination of parents whose child has epilepsy compared to parents of healthy controls revealed life stressors such as death of loved ones (n=8 vs n=4), decreased income (n=8 vs n = 4), moving (n=5 vs n=0), and relatives moving into their homes (n=10 vs n=5; Modi, 2009). Examining specific domains of family stress, Modi (2009) found that parents of children with new-onset epilepsy experienced the highest levels of stress related to finances, disciplining their child with epilepsy, concerns about education, and their marital relationships.

2.4.2 Impact of Severity of Epilepsy on the Family

Families of children with epilepsy seem to have more problems with family functioning and family stress than control families (Austin, 1988; Austin, Smith, Risinger & McNelis, 1994; Brent, Crumrine, Varma, Allan & Allman, 1987; Ferrari, Matthews & Barabas, 1983; Matthews, Barabas & Ferrari, 1982; Mims, 1997; Oostrom et al., 2003; Ritchie, 1981). For example, in a systematic review of family functioning across five samples with different pediatric chronic illnesses, including epilepsy, compared to healthy controls, Herzer et al. (2010) found that between 13% and 36% of families endorsed levels of functioning in the "unhealthy" range, with the greatest proportions in the following domains: communication, family roles, and affective involvement. However, little research has been done on the effects of *severity* of epilepsy on the family specifically.

Austin and Caplan (2007) synthesized the literature and identified clinical aspects of epilepsy such as seizure frequency, type of epilepsy, age of onset, duration of illness, and anti-epileptic drugs (AED) that were associated with family stressors, where family stressors included stressful life events and psychopathology in a family member. Mims (1997) also found that compared to families with a healthy child (p=0.03) and families with a child who had infrequent seizures (p=0.02), families with a child who had frequent seizures experienced more stress. In a cross-sectional study, Datta et al. (2006) surveyed 132 families who had a child with epilepsy. The clinical aspects of epilepsy identified as having the largest impact on families were higher frequency of seizures (p=0.002) and children taking multiple AEDs (p=0.006). Also, fewer years since diagnosis of epilepsy (p=0.05) and fewer months since last seizure (p<0.001) were associated with high impact on families (Datta et al., 2006). The few studies assessing the impact of severity of epilepsy and the family may show that the more severe the child's disability, the greater the demands and the subsequent response from the whole family (McCubbin, 1988).

From research summarized in sections 2.4.1 and 2.4.2 addressing the burden of a diagnosis of epilepsy and unpredictability of the condition on the family, there is

potential that the more severe the clinical characteristics of the child's epilepsy, the more demands and less functioning are experienced by the family.

2.5 Family Factors and Cognitive Functioning in Children with Epilepsy

Family environment may have an important influence on the course of chronic illness and the impact of the condition (Ellis et al., 2000). Family variables of closeness, caregiver coping skills, mutually supportive family relationships, clear family organization, and direct communication about the illness and its management have been consistently linked with better family and patient outcomes (Grey et al., 2006).

The role of family factors and cognitive functioning has not been fully explored in the literature. However, the few studies that include family variables (parenting, family stress, and family competence) have found significant relationships with cognitive functioning (Jones et al., 2010; Oostrom et al., 2003). To provide a rationale for exploring the relationship between family factors and cognitive functioning further, additional literature examining family variables and behaviour was reviewed. This was done because researchers have shown an association between cognitive functioning and behaviour in the epilepsy literature (Austin and Caplan 2007; Cornaggia, Beghi, Provenzi & Beghi, 2006). It is therefore reasonable to think that an association would exist between family factors and cognitive functioning.

2.5.1 Family Demands as a Mediator

Family demands may play a role in the relationship between severity of epilepsy and cognitive functioning. For all children, it appears that the family serves as the primary system for mediating life events. With chronic illness, the family environment retains the potential to serve either as a buffer to mediate the effects of stressors on children's psychological adaptation or as a potential stress maker for the patients (McCubbin, Patterson & Wilson, 1991). However no research has been done on the mediating effects of family factors between the relationship of severity of epilepsy and cognitive functioning.

McCagh et al. (2009) reports that children of parents who did not adjust well to the diagnosis of epilepsy, or children who had a history of family problems were at a greater risk of behavioural and cognitive deficits. In a prospective cohort study observing 51 children with epilepsy and 48 controls, Oostrom et al. (2003) found that children with parents who had difficulty continuing their habitual parenting style at epilepsy onset obtained worse scores in reaction times (p=0.01), location learning (p=0.05), and attention (p=0.01). Patients from families with problems obtained worse scores in behaviour (p=0.01) and location learning (p=0.05) than patients from families with less problems (Oostrom et al., 2003).

In an assessment of family demands as a potential stress mediator, Ferro et al. (2011) observed that family demands partially mediated the relationship between maternal depressive symptoms and child health-related quality of life (HRQL) (p=0.0006) in children with new-onset epilepsy. The proportion of the total effect mediated by family demands was 29%.

Given that no research that has been done on the mediating effects of family demands on cognitive functioning, it is important to explore the potential association further.

2.5.2 Family Functioning as a Mediator

Family functioning has been demonstrated as a determinant of overall quality of life and well-being in youth with chronic medical conditions (Herzer et al. 2010). However, no research has been done surrounding the effects of family functioning as a mediator between the relationship of severity of epilepsy and cognitive functioning.

In a cross sectional study, Thornton et al. (2008) found in a sample of 82 cognitively “normal” children with epilepsy that families of cognitively normal children with epilepsy function well, with overall family functioning not differing significantly from the normative mean (p<0.03). In a prospective cohort study, Ferro et al. (2011) examined family functioning in children with new-onset epilepsy as a mediator on the relationship between maternal depressive symptoms

and child health-related quality of life (HRQL). It was observed that family functioning partially mediated the impact of maternal depressive symptoms on child HRQL (p=0.0007). The proportion of the total effect of maternal depressive symptoms on child HRQL mediated by family functioning was 20%.

With further knowledge needed on the mediating effects of family factors, finding out the effects of family demands and family functioning on the relationship between severity of epilepsy and cognitive functioning in children with epilepsy is necessary to fill this gap.

2.5.3 Family Resources as a Moderator

Based on family stress theory, evidence supports that family resources serve as a protective factor for the chronically ill child (McCubbin & Patterson, 1983; McCubbin et al., 1991). This is because evidence has shown that this variable is largely stationary across families of chronically ill patients, meaning family resources stay relatively consistent over time. Family resources help the family cope with the demands placed on them from both the secondary stressor of severity of the illness and the events that occur in both normal and unusual circumstances that cause family stress. No studies have investigated family resources as a potential moderator on the relationship between severity of epilepsy and cognitive functioning in children with new-onset epilepsy. The present study addresses this gap in the literature. Below, the studies reviewed show that family resources can play a moderating role in other relationships in children with epilepsy.

In a cross-sectional study conducted by Fastenau et al. (2004) family mastery (FM), which is a subscale of the Family Inventory of Resources for Management (FIRM) measure, was found to have a significant moderating effect on the relationship between cognitive functioning and academic achievement in 173 children with epilepsy. The relationship between cognitive functioning and writing achievement varied depending on FM level; Verbal/Memory/Executive and Rapid Naming/Working Memory Functioning were strongly related to writing achievement in those children with less FM (i.e., with disorganization and little support at home), but cognitive deficits had little or no detrimental impact on

writing achievement for children with greater FM (i.e., with organization and strong support at home) (Fastenau et al., 2004). In another cross-sectional study, 287 children with new-onset epilepsy were examined. Baum et al. (2004) found that family resources moderated the relationship between temperament and internalizing and externalizing behaviour problems in children with epilepsy (p=0.03). There is support in the literature for the assertion that more adaptive resources in the family environment (e.g., family mastery and family esteem/communication) are associated with fewer behaviour problems in children with epilepsy (Baum et al., 2004). Ferro et al. (2011) also tested the moderating effects of family resources on the relationship between maternal depressive symptoms and child HRQL. Family resources moderated the impact of maternal depressive symptoms on child HRQL (β=0.25, p<0.024) in children with new-onset epilepsy.

2.6 Limitations of Prior Research

A number of cross-sectional studies have been conducted to examine the relationship between severity of epilepsy and cognitive functioning. Many studies have suggested that severity of epilepsy is associated with cognitive functioning; others however, have not found evidence of an association. These mixed results are likely attributable to the heterogeneity of the samples studied and the methods used. The majority of studies have evaluated patients recruited from tertiary institutions with small sample sizes. The studies have varied in their test intervals, the cognitive domains studied, neuropsychological tests used, and types of patients assessed. Cross-sectional studies do have limitations (e.g., cause and effect and undetected cohort bias effects), and although this research is also done cross-sectionally, the variables used to examine the relationships happen consecutively to ensure temporality as the data are from a longitudinal study.

The present research attempts to address the shortcomings of previous studies by examining cognitive functioning in the first two years of diagnosis. This window of time is a crucial period to utilize interventions. Also, this thesis will add to the breadth of knowledge that already exists on the association between the severity of

epilepsy and cognitive functioning in children with new-onset epilepsy. The present study also addresses a gap in knowledge on the stress mediating and moderating effects of family factors between the relationship of the secondary stressor, severity of epilepsy and the intermediate outcome of cognitive functioning, which has not been explored in the literature.

Chapter 3 – Methods

3 Data Source, Sample and Data Collection Procedure

The dataset was from the Health-Related Quality of Life in Children with Epilepsy Study (HERQULES), a multi-centre prospective cohort study that assessed the course and determinants of health-related quality of life in children with epilepsy during the first two years after diagnosis.

Data were collected at four times: baseline (as close as possible to the time of diagnosis), 6, 12, and 24-months post-diagnosis. These times were chosen on three considerations: (1) data should be collected close to diagnosis to identify the immediate impact of the event; (2) the time-points should be close enough together to avoid missing potential fluctuation in predictors and outcomes; and lastly, (3) the time-points should be separated enough to identify changes in the participants' day-to-day life.

A two-stage clustered sampling strategy was used to collect data. All paediatric neurologists practicing in Canada (n=72) were asked to participate by approaching parents of eligible patients about the study. Paediatric neurologists who agreed to participate were asked to complete a two-page assessment form to describe clinical features of a child's epilepsy. This information included severity of epilepsy, type of epilepsy syndrome, medication, adverse effects, any other co-morbid conditions, child's gender and date of birth.

Physicians in the study identified eligible patients between April 2004 and April 2007 who met the inclusion criteria (n=456). Parents of patients identified were sent a letter of information explaining the study and inviting them to participate. Parents who agreed were mailed the first questionnaire, which took 45-60 minutes to complete. Parents/caregivers who completed the questionnaire were those who self-identified as primarily responsible for the child's day-to-day care. Parents reported on their child's quality of life, family factors and perception of epilepsy care. The Tailored Design Method (TDM) (Dillman, Smyth & Christian, 2009)

was adopted to encourage a high participation rate by including systematic follow-up and reminders. The HERQULES study had approval from research ethics boards in all centres across the country.

Patient Inclusion Criteria:

1. new case of epilepsy where a diagnosis of epilepsy had not been previously confirmed: child was seen for the first time by a participating paediatric neurologist within the data collection period;

2. child was diagnosed between the ages of 4 and 12 years;

Patient Exclusion Criteria:

1. diagnosis of epilepsy had been previously confirmed by another physician;

2. diagnosed with other progressive or degenerative neurological disorder;

3. diagnosed with other major co-morbid non-neurological disorders that would have an impact on quality of life (e.g. asthma requiring daily medication, renal failure);

4. parent or caregiver had insufficient English to complete questionnaires.

3.1 Measures

3.1.1 From Physicians

3.1.1.1 Severity of Epilepsy

Physicians used the Global Assessment of Severity of Epilepsy (GASE) scale (Speechley et al., 2008) to assess severity of patients' epilepsy. This is a single-item global measure designed for neurologists to assess the overall severity of epilepsy in children. The GASE asks: "Taking into account all aspects of this patient's epilepsy, how would you rate its severity now?". The physician responds on a 7-point Likert scale ranging from 1=extremely severe to 7= not at all severe (Speechley et al., 2008). The variable was reverse coded so that 7 represented patients who had extremely severe epilepsy and 1 represented those with epilepsy

that was not at all severe. GASE has been found to have acceptable content, convergent and construct validity, as well as high intra-rater and inter-rater reliability (Speechley et al., 2008).

3.1.1.2 Seizure Type and Epileptic Syndrome

Seizure type was classified using the International League Against Epilepsy's 1981 classification of seizures (ILAE, 1981). The epileptic syndrome was classified using the ILAE 1989 classification (ILAE, 1989). The responses from physicians were used to create a summary variable classifying children as having: generalized or partial seizures or type undetermined.

3.1.1.3 Anti-epileptic drugs (AEDs)

AEDs were measured with a single item question. On the physician form, paediatric neurologists were asked to report the "number of AEDs *currently*" being taken by the patient.

3.1.1.4 Behaviour

The paediatric neurologist answered whether or not the child had behavioural problems. If the patient did not, the physician would answer no. If the child did have behavioural issues, the physician reported whether the issue was "mild", "moderate", or "severe".

3.1.2 From Parents

3.1.2.1 Cognitive Functioning

Cognitive functioning was assessed using the cognition subscale of the Quality of Life in Childhood Epilepsy (QOLCE) measure, a 23-item subscale assessing four cognitive domains: memory, attention, language, and other cognition. Higher scores on this subscale indicate better cognitive functioning. Offering evidence of construct validity, children with IQ scores < 70 scored poorer on all domains of the QOLCE cognitive functioning subscale, and 3 of the 4 domain scores were significantly lower (Sabaz, Cairns, Lawson, Bleasel & Bye, 2001). The internal consistency reliability of this subscale in the HERQULES sample was 0.94 two

years after diagnosis.

The Quality of Life in Childhood Epilepsy (QOLCE) measure (Sabaz et al., 2003) is a parent-report, epilepsy-specific measure evaluating health-related quality of life (HRQL) of children with epilepsy aged 4 to 18 years. The QOLCE contains 76 items with 16 subscales examining seven life function domains including: physical activities, social activities, cognition, well-being, behaviour, general health, and general quality of life (Sabaz et al., 2003). Items in this measure are rated on a five-point Likert scale, which are used to calculate the 16 subscale scores ranging from zero (low functioning) to 100 (high functioning). Subscale scores are averaged to produce an overall HRQL score. This measure has demonstrated acceptable construct validity, internal consistency reliability, and sensitivity to epilepsy severity (Sabaz et al., 2000). The internal consistency reliability for the HERQULES sample was 0.94 two years after diagnosis.

3.1.2.2 Family Demands

The Family Inventory of Life Events & Changes (FILE) is a 71-item self-report measure designed to assess the accumulation of normative and non-normative life events and changes experienced by families during the previous 12 months (Grotevant & Carlson, 1989). Each item to which a respondent answers "yes", is given a score of 1. The FILE assesses the "pile-up" of all the events by adding the scores from all items to obtain one overall score; this final summary score was used in analyses (Grotevant & Carlson, 1989). Instrument validity was determined by discriminant analyses between low and high-conflict families, showing that the FILE has the ability to differentiate between these families ($p < 0.01$; Frank-Stromborg and Olsen, 2003). Internal consistency reliability for the FILE assessed using Cronbach's alpha was 0.81 (Grotevant & Carlson, 1989). For the current sample the Cronbach's alpha of the FILE was 0.83 one year after diagnosis.

3.1.2.3 Family Functioning

The Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR) scale assesses satisfaction with family functioning. The responses for this five-item measure are based on a five-point Likert scale ranging from 0-4 for

each item. Higher scores indicate greater satisfaction with family functioning. The Family APGAR has been found to be valid and reliable in clinical and research settings with adults and children (Smilkstein, 1978). The internal consistency reliability in the HERQULES sample was very good with Cronbach's alpha of 0.86 one year after diagnosis.

3.1.2.4 Family Resources

The Family Inventory of Resources for Management (FIRM; McCubbin, Thompson & McCubbin, 1996) is a 68- item self-report scale to assess the resources a family has to adapt to stressful events. Two of the four subscales are used in the HERQULES questionnaire, (Family Strengths: Mastery and Health (20 items) and Extended Family Support (4 items)), because these subscales have been found to be related to adaptation in childhood epilepsy (Austin, Risinger & Beckett, 1992). The Family Strengths: Mastery and Health subscale measures three dimensions: (1) the sense of mastery over family events and outcomes, (2) family mutuality, and (3) physical and emotional health of the family. The Extended Family Social Support subscale measures the mutual help and support received from and given to relatives. Scoring procedures for the FIRM involve summing all response values, which range from 0 (not at all) to 3 (very well) to provide a total FIRM score. The FIRM has demonstrated very good reliability and has been shown to correlate with a similar measure, the Family Environment Scales (McCubbin et al., 1996; Fischer & Corcoran, 2007). Internal consistency reliability in the HERQULES sample for the FIRM was 0.79 one year after diagnosis.

3.1.2.5 Parental Depressive Symptoms

The Centre for Epidemiological Studies Depression Scale (CES-D) is a 20-item measure that was constructed to assess the depressive symptoms in the general adult population (Radloff, 1977). The scale includes items that survey motor functioning, mood, somatic complaints and interactions with others over the past four weeks. Each item is assessed using a four-point Likert scale (0-3), which is used to rate the frequency of symptoms experienced. The Likert scale ranges from "rarely or none of the time (less than one day)" to "most or all of the time (5-7

days)". Participants can obtain a final score that ranges from 0-60 with higher scores indicating more depressive symptoms. A final score of 16 or higher are identified as being at risk for clinical depression. In this sample, the internal consistency estimate is 0.77.

3.1.2.6 Parental Employment Status

The primary caregiver reported on his/her employment status and that of their spouse using a six-item scale. Parents were asked, "Which of the following best describes your current work status?" This polytomous nominal variable consisted of responses: "Not working due to my child's health", "Not working for *other* reasons", "Looking for work outside the home", "Working full or part-time (either outside the home or at a home-based business)", "Full time homemaker" and "Student". For analysis, the variable was dichotomized as 'employed' and 'not employed'.

3.1.2.7 Parental Education

The primary caregiver reported on his/her education and that of their spouse using a six-item scale. Parents were asked, "What is the highest grade of school you have completed?" This polytomous nominal variable consisted of responses: "Less than 8 years", "8-12 years", "Completed high school", "Completed vocational/technical training", "Completed college/university" and "Completed graduate school".

3.1.2.8 Income

The annual household income was obtained by a 12-item ordinal scale, asking parents, "In which category is your total yearly household income before taxes?" specifying that parents check one box only. Each item on the scale was a range of $10,000.

3.1.2.9 Marital Status

The primary caregiver reported on their marital status using a six-item scale. Parents were asked, "What is your current marital status?" specifying that parents check one box only. This polytomous nominal variable consisted of responses:

"Married", "Widowed", "Divorced", "Separated", "Remarried" and "Never married". For analysis, the variable was dichotomized as 'married' and 'not married'. The demographic variables (employment status, education, income and marital status) were adapted from previous studies that employed these measures successfully.

3.1.2.10 Child's Age and Gender

The primary caregiver reported on their child's age and gender. Parents were asked, "What is your child's date of birth?" The parent then wrote out their child's date of birth. Parents were also asked, "Is your child:" and specified whether their child is "Male" or "Female".

3.2 Distinction between Confounding and Mediation

As both confounding and mediation refer to the effect of a third variable to the exposure-outcome relationship, it is important to identify and differentiate the role of confounding and mediation. Confounders are defined as a third variable that can obscure a relationship between two variables of interest by changing the magnitude of an association, creating significant association where one does not exist, masking true associations or changing the direction of an association (Meinert, 1986). On the other hand, a mediator is defined as a mechanism by which the predictor variable is able to influence the outcome variable of interest (Baron & Kenny, 1986). Both of these concepts share considerable statistical similarities however the conceptual framework around this third variable differentiates the two terms (MacKinnon et al., 2000). A confounder is a variable that one must adjust for to estimate valid statistical inferences of predictor-outcome relationships. In contrast, a mediator refers to an intermediary step on the causal pathway between the outcome and predictor variables. In this thesis, family demands and family functioning are thought to be mediators, as opposed to confounders.

3.3 Data Quality Assurance

Epilepsy characteristics completed by paediatric neurologists were recorded at each centre and either faxed or mailed to the HERQULES office located in the

Department of Paediatrics at the Children's Hospital in London, Canada. Parent questionnaires were mailed directly to the HERQULES office where data entry, analysis, and quality control took place. Completed questionnaires received by the HERQULES office were examined to remove any information that would identify the patient and to check for missing data. Data were entered by graduate students in the Department of Epidemiology and Biostatistics, at the University of Western Ontario throughout the data collection period using Statistical Package for the Social Sciences (SPSS, Windows build 16, SPSS Inc., Chicago, IL). If any responses were not accommodated by the established coding structure, they were brought to the attention of the study coordinator and the principal investigator at regular project meetings. All decisions made during the process of entering data were recorded in a log for prompt reference by other data entry personnel. Research assistants other than those who initially entered the data performed data verification on all of the entered data. Data correction logs were maintained and the student who first entered the data made corrections. Before corrections were made, the data error entry rate was less than 1% for all time-points.

3.4 Data Analysis

Analyses were performed using Statistical Analysis Software (SAS v.9.2) statistical software. Descriptive statistics (presented as percentages and means ± standard deviations) were produced to present the sample in terms of epilepsy characteristics, family factors and children's cognitive functioning at baseline, 6, 12 and 24-months after epilepsy diagnosis. Bivariable analyses (t- and χ^2- tests) were done to compare families who completed all four data collection points to those who did not complete the study. *P*-values < 0.05 were considered statistically significant.

To obtain valid estimates of effect, potential confounding variables were tested first. The hypothesized confounders were from the 6-month time point. Two clinical variables, seizure type and anti-epileptic drug (AEDs) use were controlled for as it is widely stated in the literature that these variables have an effect on cognitive functioning (Aldenkamp & Bodde, 2005; Bhise et al. 2009; Caplan et al.

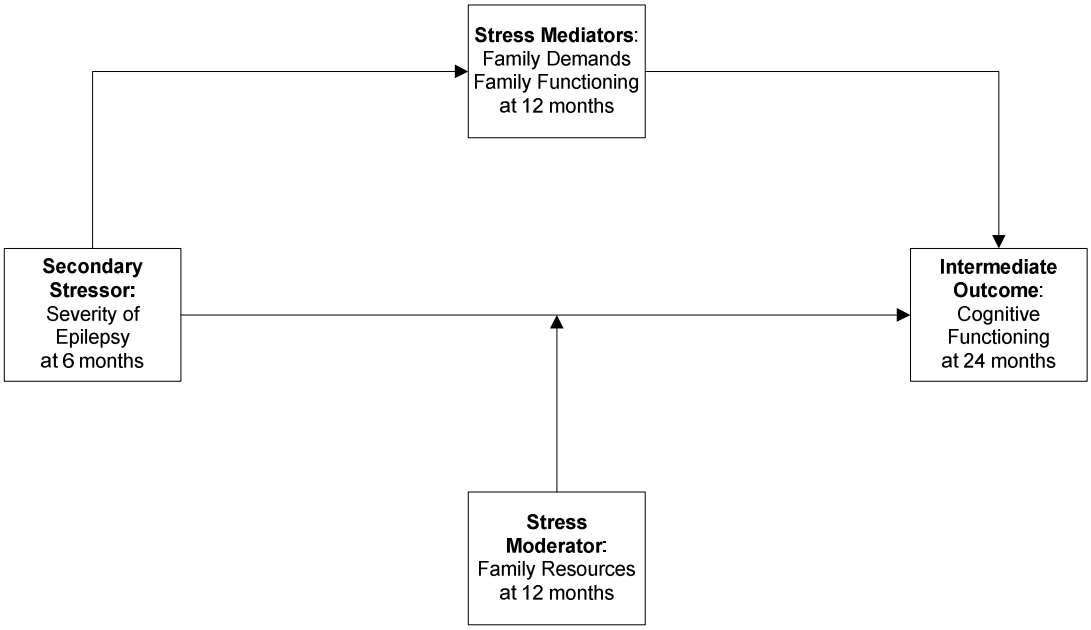
2001; Motamedi & Meador, 2003; Nolan et al. 2003). Child variables controlled for were child's age, gender and behaviour (Austin et al, 2001; Austin & Caplan 2007; Cornaggia et al, 2006; Hernandez et al, 2002; Meador et al, 2001; Oostrom et al, 2003). As stated in Chapter One, in an effort to better understand the mechanisms behind cognitive functioning in children with new-onset epilepsy, family and demographic variables were also added to the model: primary caregiver's employment status, education, depressive symptoms, marital status and annual household income.

Confounding was determined by adding the variable to the model to examine the change in the effect estimate. For the purposes of this study, a collapsibility criterion was used to operationally define confounders as those that resulted in a ≥10% change in the effect estimate of severity of epilepsy on cognitive functioning when modeled. Confounders were then added to the model in blocks starting with clinical variables, then child variables and lastly, family/demographic variables. All confounders were from the 6-month follow-up.

The choice of which time-point data to use for each variable in the analysis was based on some assumptions about the clinical scenario around the time of diagnosis and initial treatment decisions. At the initial visit to a neurologist, the type of epilepsy syndrome and severity of epilepsy is not always determined. The exposure (severity of epilepsy) as measured at the 6-month follow-up was used to allow sufficient time for the paediatric neurologist to assess the child's epilepsy severity and type, and to make treatment decisions. Severity of epilepsy measured at the 6-month follow-up was also used because literature states that even though a single seizure can alter cognitive functioning, it is frequent seizures that can have a permanent effect on cognitive functioning (Tromp et al., 2003). At the 6-month follow-up, children potentially have had more seizures allowing the assessment of the severity of epilepsy on cognitive functioning. The outcome (cognitive functioning) as assessed at the final time-point of 24-months was used to ensure temporality whereby the exposure came before the outcome. Data for family resources, demands and functioning were measured at the 12-month follow-up. One-year post diagnosis gives the family enough time to process the child's illness

and experiences associated with changes in their lives. The inclusion of the variables at these specific time-points allows a sequence of events to take place as postulated in the conceptual framework guiding this thesis. Figure 3 shows the segment of the stress process model that is explored in this thesis specifying the time-points at which the variables were assessed.

Figure 3. Segment of the Stress Process Model specifying Time-Points for Modeling



3.4.1 Objective 1 – Assessing the Relationship between Severity of Epilepsy and Cognitive Functioning

Multiple linear regressions are conducted to address Objective 1 and 2(a). This method was used because it allows the researcher to examine the independent effect of the exposure of interest while adjusting for other variables that may affect the estimate of the relationship between the exposure of interest and the outcome. Linear regressions were utilized because the outcome variable in this thesis, parent-perceived cognitive functioning, is continuous.

To address the first objective of this thesis, a multiple linear regression was performed to assess the association between severity of epilepsy 6 months after diagnosis and cognitive functioning 24 months after diagnosis. The four domains measured within the cognition subscale of the QOLCE were combined to create one summary variable of cognitive functioning at the 24-month time-point. Potential confounders were used from the 6-month follow-up and entered in blocks, starting with clinical variables, then child variables and finally family/demographic variables.

3.4.2 Objective 2a – Assessing Family Resources as an Effect Measure Modifier

Effect measure modification occurs when the strength of an association between an exposure and an outcome depends on the value of a third variable (Greenland & Morgenstern, 1989). This third variable is known as the effect measure modifier or moderator. The hypothesis associated with Objective 2(a) is that family resources may modify the association between severity of epilepsy and parent-perceived cognitive functioning.

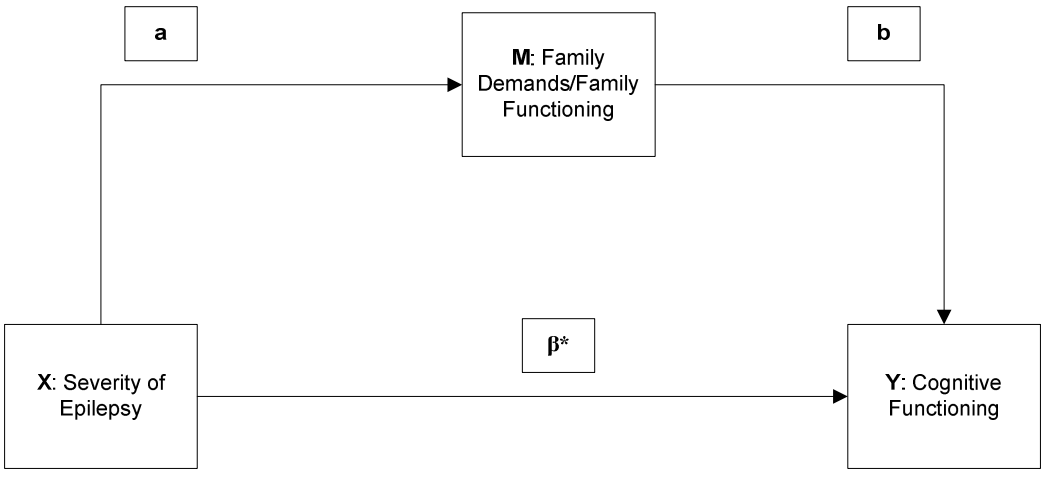
To test this hypothesis, a multiple linear regression was computed similar to that used to assess the first objective, adding an interaction term that is the product of the variable potentially being moderated (severity of epilepsy at 6 months) and the variable hypothesized to moderate (family resources at 12 months). This interaction term tested whether the effect of severity of epilepsy on cognitive functioning varied for children based on their level of family resources. If the effect of the interaction term is statistically significant ($p<0.05$) then the direct relationship between severity of epilepsy and parent-perceived cognitive functioning is dependent upon the level of family resources.

3.4.3 Objectives 2b and c – Assessing Family Demands and Family Functioning as Mediators

A mediator can be explained as the carrier of information along the causal chain of effects (Little et al., 2007). Baron and Kenny (1986) suggested three necessary but not sufficient conditions for mediation: (1) the exposure of interest (X) is

significantly related to the mediator (M); (2) the mediator is significantly related to the outcome of interest (Y); (3) the relationship between the exposure and the outcome diminishes when the mediator is included in the model. There were two potential mediators of interest in this thesis, family demands and family functioning, which were analyzed in separate models. According to the criteria proposed by Baron and Kenny (1986), mediation would be claimed if: (1) severity of epilepsy (X) is significantly related to family demands (M); (2) family demands are significantly related to parent-perceived cognitive functioning (Y); (3) the relationship between severity of epilepsy and parent-perceived cognitive functioning diminishes when the variable family demands is entered in the model. Similarly, (1) severity of epilepsy (X) is significantly related to family functioning (M); (2) family functioning is significantly related to parent-perceived cognitive functioning (Y); (3) the relationship between severity of epilepsy and parent-perceived cognitive functioning diminishes when family functioning is entered in the model. Full mediation would be concluded if the inclusion of family demands or family functioning decreased the effect of severity of epilepsy on cognitive functioning to zero. Partial mediation would be concluded if the effect of severity of epilepsy on cognitive functioning decreased by a non-trivial amount, but not to zero when family demands or family functioning was added into the model.

Figure 4. Illustration of a Mediation Design



In Figure 4, the indirect effect is defined as the product of the X → M path (*a*) and the M → Y path (*b*), or *ab* and the direct effect path is the product of X→Y (*β**). It

is well known that for linear models c-c'=ab (MacKinnon & Dwyer, 1993). Where c denotes the direct relationship between X and Y in an unmediated model and where c' denotes the relationship between X and Y in a model where there is a hypothesized mediator.

It has been suggested that direct application of Baron and Kenny's (1986) multiple test estimates underestimates the standard errors (Cerin, Taylor, Leslie & Owen, 2006), so a more rigorous method for testing H_0: c-c'=0 (Schluchter, 2008) was adopted in this thesis. Specifically, the problem amounts to testing the difference between the coefficients for severity of epilepsy with and without the potential mediator (M) in the multiple linear models, i.e., H_0: $\beta-\beta^*=0$.

(1) with M: $Y=\beta_0^*+\beta^*X+\gamma M$ + confounders

(2) without M: $Y=\beta_0+\beta X$ + confounders

To more accurately estimate the standard error of the estimated difference, Schluchter (2008) made the suggestion to use robust estimators with the generalized estimating equations (GEE) approach for variances of β estimate and β^* estimates, as well as for their covariance (because the same dataset is used for estimating β and β^*). For this purpose, two copies of data for each subject need to be created as follows where ID is the observation, Y is the outcome, X is the exposure, M* is the mediator and G is the indicator variable:

ID	Y	X	M*	G
1	Y_1	X_1	0	0
1	Y_1	X_1	M_1	1
2	Y_2	X_2	0	0
2	Y_2	X_2	M_2	1
n	Y_n	X_n	0	0

n	Y_n	X_n	M_n	1

The augmented dataset can then be fitted to a linear model of:

(3) $Y=\beta_0 + \beta_1 X + \theta G + \theta_0 XG + \gamma M^*$

Where the coefficient for the interaction term is the indirect effect:

$\theta_0= \beta - \beta^*$

This is the case because when G=0, M*=0, equation (3) reduces to:

$Y= \beta_0 + \beta_1 X$

and when G=1, M=M, equation (3) reduces to:

$Y= \beta_0 + \beta_1 X + \theta + \theta_0 X + \gamma M$

$= \beta_0 + \theta + (\beta_1 + \theta_0) X + \gamma M$

Corrected standard errors for the difference can then be obtained using SAS GENMOD implementation of the GEE approach. When using this approach, the parameters $\theta_1 \ldots \theta_n$ are the differences between the estimates of the regression coefficients of $X_1 \ldots X_n$ in the full and mediated models. In other words, the G*Severity of Epilepsy variable within the model is the difference between the models with and without the potential mediators. Schluchter (2008) has shown the validity of this approach using simulation evaluations. The Sobel (1982) test also was conducted to assess mediation.

Chapter 4 – Results

4 Chapter Overview

This chapter presents the findings. Section 4.1 provides a description of the sample characteristics of both parents and children, and includes an attrition analysis. In the following sections (4.2-4.5), the findings for each individual study objective are presented.

4.1 Sample Characteristics

A total of 53 out of 72 eligible paediatric neurologists (74%) agreed to participate and recruited patients. Paediatric neurologists identified 456 eligible patients whose parents were approached to participate, and of these, 374 (82%) completed the baseline questionnaire and 283 (76%) of those parents were retained to the final 24-month follow-up.

A comparison of parents who were retained for the entire study and those lost to follow-up is provided in Table 1. The two groups did not differ on key epilepsy factors such as type of epilepsy (p=0.40), current AED use (p=0.60), and severity of epilepsy (p=0.85). However, primary caregivers who did not complete the study were more likely to be unmarried (p<0.05), have a lower annual household income (p=0.01), to be less educated (p<0.05) and more likely to have a child with cognitive problems as reported by their paediatric neurologist (p=0.04). Also, those families who were lost to follow-up had more family demands (p<0.05), and fewer family resources (p=0.01).

A description of the children's characteristics at each time-point is provided in Table 2. At baseline, the mean age (standard deviation) of children in the sample was 7.4 (2.4) years and approximately half (52%) of the children in the sample were males. The majority (54%) of children were reported by their neurologists as having either "a little severe" or "not at all severe" epilepsy. Approximately 60% of children had partial seizures, 38% had generalized seizures and for 2% the type of seizure was undetermined. Approximately 67% of children were currently on one

or more anti-epileptic drugs (AED). In addition, on average, parents reported that children had generally good cognitive scores, with a mean score of 67.0 (21.2), on the cognitive functioning subscale of the QOLCE.

Table 3 provides a description of parent and family characteristics. Of participating parents, 81% were currently married. There was considerable variation in annual household income for this sample with a range of less than $10,000 (2%) to $100,000 or more (22%). The majority of primary caregivers had completed college/university (54%), and 67% were employed either full-time or part-time. Of their partners, 51% had completed college/university and 88% were employed either full-time or part-time. Families had adequate resources with a mean score of 50.0 (11.1) on the Family Inventory of Resources and Management (FIRM) scale. On average, families had low demands with a mean score of 10.0 (6.5) on the Family Inventory of Life Events and Changes (FILE) measure. Lastly, family functioning as measured by the Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR) was good on average with a mean score of 14.0 (3.8).

4.2 Objective 1 – Assessing the Relationship between Severity of Epilepsy and Cognitive Functioning

To examine whether severity of epilepsy affected parent-perceived cognitive functioning, severity of epilepsy at 6-months was the independent variable of interest and parent-perceived cognitive functioning at 24 months was the dependent variable. Multiple linear regression analyses were conducted, controlling for the potential confounding variables of seizure type, anti-epileptic drug use, age, gender and behaviour of the child, annual household income, marital status and primary caregiver employment status, depressive symptoms and education. The results of the multiple regression analyses are presented below in Table 4. Confounders were added in blocks starting with clinical variables (model 2), then child variables (model 3) and lastly, family and demographic variables (model 4).

Model 4 represents the final model for this objective. Severity of epilepsy at 6-months had a significant negative effect on parent-perceived cognitive functioning

at 24-months with an adjusted parameter estimate of -3.84 (95% CI: -6.25, -1.44) for a one-unit increase on the GASE score (p<0.05).

4.3 Objective 2a – Assessing Family Resources as an Effect Measure Modifier

The potential moderating effect of family resources on the relationship between severity of epilepsy and parent-perceived cognitive functioning was examined by including an interaction term between severity of epilepsy at 6 months and the moderator (family resources) at 12 months (model 1). An interaction term was added into the model along with potential confounders. Again, confounders were added in blocks starting with clinical variables (model 2), then child variables (model 3) and family/demographic variables entered last (model 4). The results for model 1-4 are presented in Table 5.

The interaction term indicated that the effect measure modifier was statistically significant with a parameter estimate of -0.23 (95% CI: -0.44, -0.02) denoting that the relationship between severity of epilepsy and parent-perceived cognitive functioning was dependent on the level of family resources (p=0.03).

Post-hoc testing of the significant moderating effect of family resources on the relationship between severity of epilepsy and parent-perceived cognitive functioning was done to determine the conditions that dictate where the differences in the interaction term occur. (Holmbeck, 2002; Aiken & West, 1991). The technique introduced by Holmbeck (2002) was used. This method is designed to interpret the interaction effect of two continuous variables.

All variables in the original model were centered and two new variables, low resources and high resources, were created based on the mean and standard deviations (SD) of the FIRM variable. 'LOWFIRM' equals 0 when FIRM is 1 SD below the mean and 'HIGHFIRM' equals 0 when FIRM is 1 SD above the mean. We also computed two new interaction terms between the new variables and the severity of epilepsy measure (LOWFIRM*GASE and HIGHFIRM*GASE). Two

regressions were run to establish the slope for those with low resources and those with high resources and two equations were generated from the analysis.

The results of the two regressions were plotted in Figure 5 to illustrate the moderating effect of family resources. The diagram shows that at low levels of epilepsy severity, higher cognitive functioning scores are reported for children in families with more family resources. However, among children with more severe epilepsy, the effect of family resources is significantly reduced.

4.4 Objective 2b –Assessing Family Demands as a Mediator

The potential mediating effect of family demands measured 12 months post diagnosis was entered into a generalized estimating equations (GEE) model, measuring the relationship between severity of epilepsy at 6 months post diagnosis and parent-perceived cognitive functioning at 24 months after diagnosis.

A preliminary analysis was done with multiple linear regression models to compare the total effect to the direct effect. The assessment of total effect included all the same variables analyzed for the other objectives (severity of epilepsy as the independent variable of interest, seizure type, anti-epileptic drug use, child's age, gender, and behaviour as well as annual household income, marital status, primary caregiver's employment status, education and depressive symptoms. The assessment of direct effect included the variables stated above and the potential mediator (family demands).

Results from the preliminary analysis showed that the estimate of the total effect of severity of epilepsy was -3.81 (95% CI: -6.23, -1.40). The direct effect of severity of epilepsy when adding family demands into the model was -3.61 (95% CI: -6.00, -1.21). The magnitude of the indirect effect is calculated by subtracting the direct effect from the total effect. The total-direct effect is -0.20, which reduces the estimate of severity of epilepsy by approximately 17%.

The GEE model is presented below in Table 6. In Table 6, G represents the indicator variable, G*variable are interaction terms and Mstar is the mediator.

Similar to the previous objectives, confounders were entered into the model by blocks. First clinical variables were added (model 1), then child variables (model 2) and lastly family/demographic variables (model 3). G*Severity of epilepsy denotes the difference in coefficients (indirect effect) of the equations Y regressed on X and covariates to Y regressed on X, M, and covariates ($\theta = \beta - \beta^*$). In other words, G*Severity of epilepsy is the difference between having the mediator (family demands) in the model and not having the mediator in the model.

Family demands did not mediate the impact of severity of epilepsy on parent-perceived cognitive functioning (ab= 0.21, SE=0.21, p=0.32). Since the Sobel (1982) test has been widely used in the social sciences to measure mediation effects, it was conducted as well to test the mediating effect of family demands and confirmed that the mediating effect of family demands was not significant (data not shown).

4.5 Objective 2c – Assessing Family Functioning as a Mediator

The potential mediating effect of family functioning was also entered into a GEE model. Similar steps taken in objective 2(b) were replicated for objective 2(c). As reported for objective 2(c), the preliminary analysis for the total effect of severity of epilepsy on cognitive functioning produced an estimate of -3.81 (95% CI: -6.23, -1.40). The direct effect when adding the potential mediator, family functioning was -3.66 (95% CI: -6.09, -1.23). The total-direct effect is -0.15, which reduces the estimate of severity of epilepsy by approximately 11%. The GEE model is presented in Table 7.

The difference between the coefficients (Y regressed on X, and Y regressed on X and M) provided by the parameter G*Severity of epilepsy indicates that family functioning did not significantly mediate the relationship between severity of epilepsy and parent-perceived cognitive functioning (ab=0.15, SE=0.17, p=0.35). The Sobel (1982) test was conducted as well and confirmed that the mediating effect of family functioning was not significant (data not shown).

Table 1. Comparison of Parents Completing Study and Lost to Follow-Up

	Completed Follow-Up (n=268)	Lost to Follow-Up (n=89)	t/χ^2	P-value
Seizure Type				
Generalized	37.3	42.9	0.79	0.40
Partial	62.7	57.1		
Current AED use	75.0	79.0	-0.52	0.60
Epilepsy Severity	5.43	5.40	0.19	0.85
Marital Status				
Married	84.2	70.0	8.34	0.0003
Not Married	17.0	31.4		
Annual Household Income				
< $20,000	6.1	14.8	14.07	0.01
$20,000-39,999	12.7	18.7		
$40,000-59,999	23.3	17.5		
$60,000-79,999	17.0	24.1		
≥$80,000	41.4	26.7		
Unknown	2.8	1.9		
Education				
Primary School	9.1	21.6	11.06	0.002
High School	21.2	24.3		
Technical Training	14.9	11.8		
College/University	57.5	45.0		
Employment Status				
Not Employed	8.1	15.8	5.31	0.002
Employed	69.2	58.9		
Homemaker	23.1	24.7		
Student	1.7	3.0		
Family Demands mean (SD)	8.95 (6.3)	11.19 (7.5)	-2.87	0.004
Family Resources mean (SD)	50.91 (11.5)	47.52 (10.4)	2.55	0.01
Family Functioning mean (SD)	14.11 (3.9)	13.35 (3.5)	1.69	0.09

* Reported as percentages, unless otherwise stated

Table 2. Child Characteristics of Study Sample at Each Time-Point

Child Factors		Baseline (n=374)	6 month (n=336)	12 month (n=304)	24 month (n=282)
Age, years	mean (SD)	7.4 (2.4)	7.9 (2.4)	8.4 (2.4)	9.4 (2.4)
Sex	Male	52.0	51.0	50.0	52.0
Epilepsy severity					
Extremely to Quite severe		6.1	3.2	2.1	2.1
Moderately to Somewhat severe		40.6	22.6	19.3	13.6
A little severe		36.0	30.5	31.7	26.3
Not at all severe		17.3	43.6	46.9	57.9
Seizure type					
Partial		60.5	59.8	59.3	57.8
Generalized		37.7	38.5	39.0	39.5
Undetermined		1.8	1.7	1.7	2.6
Current AED use		67.0	80.0	82.0	77.0
QOLCE	mean (SD)				
Cognition subscale		67.0 (21.2)	69.0 (20.4)	68.0(20.8)	69.0 (20.6)

*Reported as percentages, unless otherwise stated
*Children in the sample were 4 to 12 years of age
*The QOLCE Cognition subscale is scored within the range of 0 to 100

Table 3. Parent and Family Characteristics of Study Sample at Each Time-Point

Family Factors	Baseline (n=374)	6 month (n=336)	12 month (n=304)	24 month (n=282)
Marital Status				
Married	79.7	79.2	80.3	82.3
Never married	9.4	8.6	7.9	6.0
Separated	4.8	7.1	6.6	6.4
Divorced	4.6	3.6	3.9	4.3
Remarried	1.1	0.3	0.7	0.0
Widowed	0.5	0.6	0.7	0.7
Annual Household Income				
Less than $20,000	7.5	9.0	4.9	3.5
$20,000-$39,999	13.4	12.5	13.8	10.6
$40,000-$59,999	20.6	18.7	16.8	17.6
$60,000-$79,999	18.2	16.3	16.7	18.8
$80,000 or more	34.8	37.2	40.7	41.4
Education – Primary caregiver				
Less than 8 years	1.9	0.6	0.3	0.4
8-12 years	9.4	8.0	6.2	5.3
High school	22.2	21.1	19.7	19.5
Vocational/Technical training	13.1	10.7	13.8	11.4
College/University	44.7	48.8	50.8	51.8
Graduate school	8.8	8.3	8.9	11.7
Employment status – Primary caregiver				
Employed	66.6	69.6	73.1	75.9
Full-time homemaker	21.4	19.1	18.7	15.3
Not working	7.5	5.7	4.6	4.3
Looking for work outside home	1.9	2.1	0.7	2.5
Student	1.9	2.1	2.3	0.7
Education – Spouse				
Less than 8 years	1.5	1.4	0.4	0.4
8-12 years	13.3	9.5	11.4	9.3
High school	22.8	23.2	20.5	24.6
Vocational/technical training	19.4	17.5	20.2	16.9
College/university	31.8	37.1	36.5	37.5
Graduate school	10.2	10.5	10.7	10.9

Family Factors	**Baseline (n=374)**	**6 month (n=336)**	**12 month (n=304)**	**24 month (n=282)**
Employment status – Spouse				
Employed	88.0	90.9	90.1	91.5
Full-time homemaker	3.7	2.1	2.7	3.2
Not working	5.3	4.9	4.6	3.6
Looking for work outside home	1.5	1.4	1.9	0.8
Student	0.3	0.4	0.4	0.8
Resources, FIRM mean (SD)	50.0 (11.1)	51.0 (11.2)	51.0 (11.5)	51.0 (11.5)
Demands, FILE mean (SD)	10.0 (6.5)	N/A	8.0 (6.1)	8.0 (5.7)
Functioning, APGAR mean (SD)	14.0 (3.8)	14.0 (3.7)	14.0 (4.0)	14.0 (3.9)

*Reported as percentages, unless otherwise stated
*Family Inventory of Resources for Management (FIRM) is scored within the range of 16 to 72
*Family Inventory of Life Events & Changes (FILE) is scored within the range of 0 to 55
*Family Adaptability, Partnership, Growth, Affection and Resolve (APGAR) is scored within the range of 1 to 20

Table 4. Regressions of Severity of Epilepsy on Cognitive Functioning

	Model 1 β (SE) 95% CI	Model 2 β (SE) 95% CI	Model 3 β (SE) 95% CI	Model 4 β (SE) 95% CI
Intercept	72.60 (1.78)** 69.09, 76.10	68.58 (5.09)** 58.55, 78.60	56.73 (7.79)** 41.39, 72.08	67.64 (8.88)** 50.14, 85.14
Severity of Epilepsy	-3.41 (1.22)* -5.81, -1.01	-3.94 (1.28)* -6.45, -1.42	-3.99 (1.26)* -6.48, -1.50	**-3.84 (1.22)*** **-6.25, -1.44**
Seizure Type		1.28 (2.73) -4.11, 6.67	1.77 (2.71) -3.57, 7.11	2.73 (2.59) -2.37, 7.83
Current AED use		2.23 (1.52) -0.76, 5.21	2.33 (1.50) -0.62, 5.29	2.91 (1.54) -0.13, 5.94
Child's Age			1.14 (0.57)* 0.02, 2.27	1.24 (0.55)* 0.17, 2.32
Child's Gender			1.80 (2.64) -3.41, 7.01	1.81 (2.50) -3.11, 6.73
Child's Behaviour			-0.48 (0.21)* -0.88, -0.07	-0.37 (0.20) -0.76, 0.02
Primary Caregiver's Employment Status				-1.63 (2.75) -7.06, 3.79
Primary Caregiver's Education				0.01 (0.08) -0.16, 0.17
Primary Caregiver's Depressive Symptoms				-0.76 (0.14)** -1.04, -0.48
Marital Status				-3.90 (3.39) -10.58, 2.77
Annual Household Income				0.06 (0.06) -0.06, 0.18

**P<0.0001, *p<0.05

Table 5. Moderating effect of Family Resources on Relationship between Severity of Epilepsy and Cognitive Functioning

	Model 1 **β (SE)** **95% CI**	**Model 2** **β (SE)** **95% CI**	**Model 3** **β (SE)** **95% CI**	**Model 4** **β (SE)** **95% CI**
Intercept	48.83 (8.22)** 33.95, 66.07	48.90 (9.14)** 30.89, 66.91	32.93 (10.81)* 11.63, 54.23	59.79 (13.00)** 34.17, 85.41
Severity of Epilepsy	-9.87 (5.62) -20.94, 1.20	-9.97 (5.64) -21.08, 1.14	-11.34 (5.62)* -22.41, -0.27	-14.90 (5.57)* -25.88, -3.92
Family Resources	1.44 (0.66)* 0.13, 2.74	1.40 (0.67)* 0.09, 2.72	1.61 (0.67)* 0.30, 2.92	1.74 (0.66)* 0.44, 3.03
Severity of Epilepsy x Family Resources	-0.14 (0.11) -0.35, 0.07	-0.14 (0.11) -0.35, 0.08	-0.16 (0.11) -0.38, 0.05	**-0.23 (0.11)*** **-0.44, -0.02**
Seizure Type		-0.34 (2.60) -5.47, 4.79	-0.20 (2.58) -5.28, 4.89	1.01 (2.57) -4.06, 6.07
Current AED use		1.06 (1.46) -1.83, 3.94	1.20 (1.45) -1.66, 4.06	2.10 (1.56) -0.98, 5.17
Child's Age			1.40 (0.55)* 0.33, 2.48	1.26 (0.54)* 0.20, 2.32
Child's Gender			2.57 (2.53) -2.41, 7.56	3.00 (2.47) -1.87, 7.87
Child's Behaviour			-0.09 (0.14) -0.37, 0.19	-0.11 (0.14) -0.39, 0.16
Primary Caregiver's Employment Status				-4.65 (2.74) -10.04, 0.74
Primary Caregiver's Education				0.02 (0.08) -0.14, 0.18
Primary Caregiver's Depressive Symptoms				-0.58 (0.16)* -0.90, -0.27
Marital Status				-1.17 (3.38) -7.83, 5.50
Annual Household Income				0.07 (0.06) -0.05, 0.19

**P<0.0001, *p<0.05

Table 6. Mediating effect of Family Demands on Relationship between Severity of Epilepsy and Cognitive Functioning.

	Model 1 β (SE) 95% CI	Model 2 β (SE) 95% CI	Model 3 β (SE) 95% CI
Intercept	70.80 (2.48)** 65.94, 75.65	60.24 (5.65)** 49.17, 71.31	72.71 (6.97)** 59.05, 86.37
Severity of Epilepsy	-3.91 (1.35)* -6.56, -1.26	-3.96 (1.33)* -6.57, -1.35	-3.81 (1.30)* -6.35, -1.27
Seizure Type	-1.07 (2.65) -6.26, 4.13	-1.58 (2.59) -6.65, 3.50	-2.56 (2.50) -7.47, 2.33
Current AED use	2.31 (1.36) -0.35, 4.97	2.40 (1.35) -0.24, 5.06	2.97 (1.45)* 0.13, 5.83
Child's Age		1.11 (0.55)* 0.04, 2.19	1.22 (0.52)* 0.20, 2.24
Child's Gender		1.76 (2.65) -3.43, 6.96	1.74 (2.49) -3.14, 6.61
Child's Behaviour		-0.47 (0.05)** -0.58, -0.37	-0.37 (0.06)** -0.48, -0.25
Primary Caregiver's Employment Status			-1.48 (2.70) -6.79, 3.82
Primary Caregiver's Education			0.01 (0.06) -0.11, 0.13
Primary Caregiver's Depressive Symptoms			-0.76 (0.15)** -1.04, -0.47
Marital Status			-3.73 (3.29) -10.18, 2.71
Annual Household Income			0.06 (0.05) -0.04, 0.16
G	8.68 (2.14)** 4.48, 12.88	8.29 (2.67)* 3.04, 13.52	2.94 (1.87) -0.72, 6.60
G*Severity of Epilepsy	0.53 (0.37) -0.18, 1.25	0.51 (0.35) -0.19, 1.20	**0.21 (0.21)** **-0.20, 0.61**
G*Seizure Type	-0.61 (0.79) -2.17, 0.94	-0.52 (0.75) -1.99, 0.95	-0.14 (0.38) -0.89, 0.61
G*Current AED use	-0.91 (0.40)* -1.68, -0.13	-0.87 (0.39)* -1.63, -0.10	-0.48 (0.31) -1.09, 0.13

	Model 1 β (SE) 95% CI	Model 2 β (SE) 95% CI	Model 3 β (SE) 95% CI
G*Child's Age		-0.02 (0.15) -0.32, 0.27	-0.03 (0.08) -0.17, 0.12
G*Child's Gender		0.03 (0.74) -1.42, 1.49	0.02 (0.36) -0.69, 0.73
G*Child's Behaviour		0.09 (0.02)** 0.05, 0.14	0.03 (0.01)* 0.00, 0.06
G*Primary Caregiver's Employment Status			-0.22 (0.42) -1.05, 0.60
G*Primary Caregiver's Education			-0.01 (0.01) -0.04, 0.01
G*Primary Caregiver's Depressive Symptoms			0.14 (0.08) -0.01, 0.29
G*Marital Status			0.58 (0.59) -0.58, 1.73
G*Annual Household Income			-0.01 (0.01) -0.02, 0.01
Mstar	-1.01 (0.22)** -1.45, -0.57	-0.97 (0.22)** -1.41, -0.53	-0.53 (0.23)* -0.98, -0.09

**P<0.0001, *p<0.05

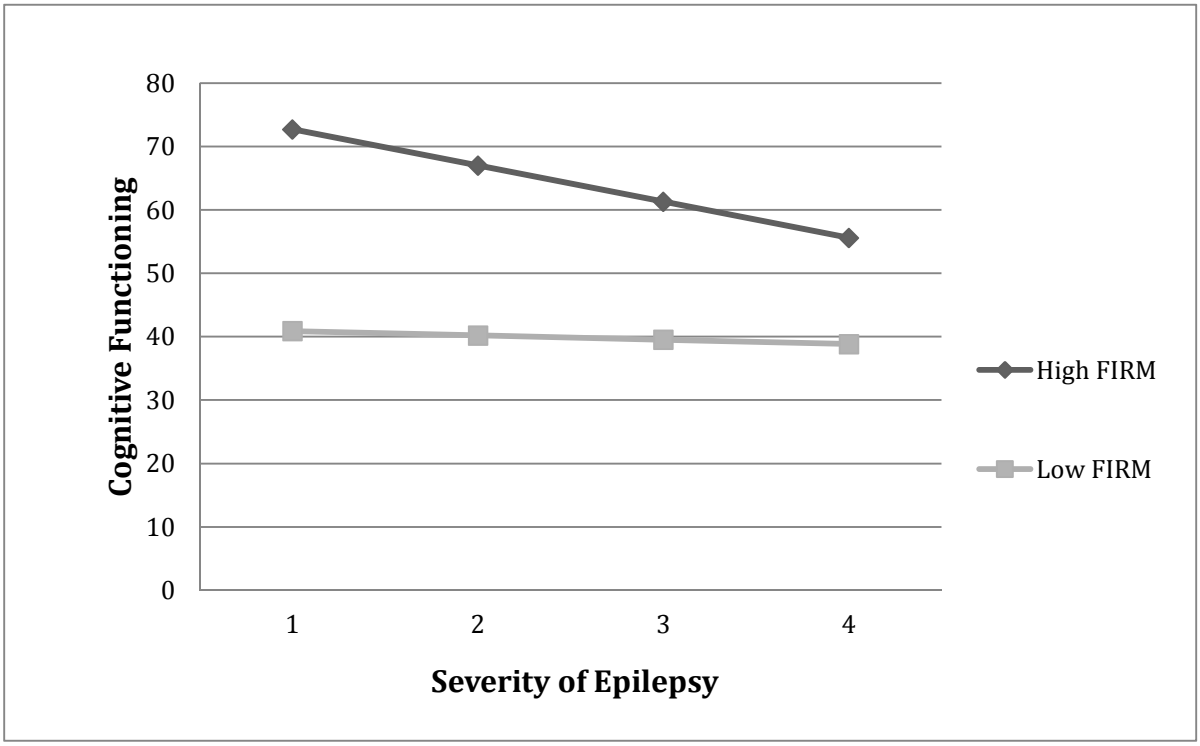
Table 7. Mediating effect of Family Functioning on Relationship between Severity of Epilepsy and Cognitive Functioning

	Model 1 β (SE) 95% CI	Model 2 β (SE) 95% CI	Model 3 β (SE) 95% CI
Intercept	70.80 (2.48)** 65.94, 75.65	60.24 (5.65)** 49.17, 71.31	72.71 (6.97)** 59.05, 86.37
Severity of Epilepsy	-3.91 (1.35)* -6.56, -1.26	-3.96 (1.33)* -6.57, -1.35	-3.81 (1.30)* -6.35, -1.27
Seizure Type	-1.07 (2.65) -6.26, 4.13	-1.58 (2.59) -6.65, 3.50	-2.56 (2.50) -7.47, 2.33
Current AED use	2.31 (1.36) -0.35, 4.97	2.40 (1.35) -0.24, 5.06	2.97 (1.45)* 0.13, 5.83
Child's Age		1.11 (0.55)* 0.04, 2.19	1.22 (0.52)* 0.20, 2.24
Child's Gender		1.76 (2.65) -3.43, 6.96	1.74 (2.49) -3.14, 6.61
Child's Behaviour		-0.47 (0.05)** -0.58, -0.37	-0.37 (0.06)** -0.48, -0.25
Primary Caregiver's Employment Status			-1.48 (2.70) -6.79, 3.82
Primary Caregiver's Education			0.01 (0.06) -0.11, 0.13
Primary Caregiver's Depressive Symptoms			-0.76 (0.15)** -1.04, -0.47
Marital Status			-3.73 (3.29) -10.18, 2.71
Annual Household Income			0.06 (0.05) -0.04, 0.16
G	-14.32 (4.40)* -22.93, -5.70	-15.19 (4.81)* -24.61, -5.77	-6.09 (5.32) -16.51, 4.34
G*Severity of Epilepsy	0.41 (0.28) -0.35, 0.96	0.39 (0.28) -0.15, 0.93	**0.15 (0.17)** **-0.17, 0.48**
G*Seizure Type	0.48 (0.57) -0.63, 0.96	0.48 (0.56) -0.62, 1.58	0.28 (0.32) -0.35, 0.92
G*Current AED use	-0.46 (0.30) -1.03, -0.13	-0.44 (0.28) -1.00, 0.11	-0.24 (0.24) -0.71, 0.22

	Model 1 β (SE) 95% CI	Model 2 β (SE) 95% CI	Model 3 β (SE) 95% CI
G*Child's Age		0.05 (0.10) -0.15, 0.26	0.00 (0.04) -0.07, 0.07
G*Child's Gender		0.37 (0.54) -0.69, 1.42	0.15 (0.21) -0.27, 0.57
G*Child's Behaviour		0.05 (0.02)* 0.01, 0.08	0.01 (0.01) -0.01, 0.03
G*Primary Caregiver's Employment Status			-0.20 (0.28) -0.74, 0.34
G*Primary Caregiver's Education			0.01 (0.01) -0.01, 0.02
G*Primary Caregiver's Depressive Symptoms			0.05 (0.05) -0.04, 0.15
G*Marital Status			0.39 (0.46) -0.58, 1.73
G*Annual Household Income			-0.01 (0.01) -0.02, 0.01
Mstar	1.01 (0.31)* 0.41, 1.62	1.00 (0.22)* -1.41, -0.53	0.32 (0.32) -0.28, 0.99

**P<0.0001, *p<0.05

Figure 5. Moderating effect of Family Resources on the Relationship between Severity of Epilepsy and Cognitive Functioning



Chapter 5 - Discussion

5 Chapter Overview

This chapter summarizes the findings related to each objective and discusses their implications. Section 5.2 and 5.3 describe the strengths and weaknesses associated with the study. Finally, in section 5.4, recommendations for future research are made.

5.1 Summary of Results

This thesis assessed the association between the severity of epilepsy and parent-perceived cognitive functioning in children with new-onset epilepsy. In addition, it assessed the potential role of family resources as a moderator and family demands and family functioning as mediators of the relationship between severity of epilepsy and parent-perceived cognitive functioning. This thesis was guided by the Stress Process Model, which examines the ways in which stressors mediate and moderate the association between social structure and an array of health outcomes. The study sample consisted of children 4-12 years of age collected through a multi-centre prospective cohort study, Health Related Quality of Life in Children with Epilepsy (HERQULES). To our knowledge, this is the first study to examine the moderating and mediating effects of family factors on the relationship between severity of epilepsy and cognitive functioning in children with epilepsy.

5.1.1 Objective 1- Severity of Epilepsy and Cognitive Functioning

This objective assessed the relationship between severity of epilepsy 6 months after diagnosis and parent-perceived cognitive functioning 24 months after diagnosis. It was hypothesized that the more severe epilepsy a child had, the poorer his/her cognitive functioning would be. The rationale behind this objective was that frequent seizures can interfere with brain development (Aldenkamp, 1997). Recent studies have established that even single seizures can lead to a temporary change in cognitive performance but that changes persist over time only when the frequency of seizures are high or postictal effects are prolonged (Tromp et al. 2003).

This hypothesis was supported. Severity of epilepsy six months after diagnosis was inversely associated with cognitive functioning two years after diagnosis. Children with more severe epilepsy had worse cognitive functioning scores. This is consistent with prior literature in this area. Hermann et al. (2006) found that cognitive functioning in children with new or recent-onset epilepsy was adversely affected early in the course of the disease, regardless of the type of syndrome. These children not only had impairments in intelligence, but also language, executive function and memory. Other studies have also shown that frequent seizures were associated with significantly worse cognitive functioning in comparison to those with infrequent seizures and healthy controls (Bjornaes et al, 2001; Nolan et al, 2003; Souza-Oliveira et al, 2010).

The fact that severity of epilepsy as evaluated by neurologists approximately six months after the child's diagnosis is predictive of cognitive functioning two years after diagnosis could help health care providers and parents envision what outcomes may lay ahead to assist them in proactively planning to support children's needs.

5.1.2 Objective 2(a) – Family Resources as a Moderator

The second objective of this thesis was to examine the potential moderating effect of family resources on the relationship between severity of epilepsy and parent-perceived cognitive functioning. No previous research has explored family resources as a potential moderator on the relationship between severity of epilepsy and cognitive functioning. It has been shown, however, that family resources can help the family cope with the demands placed on them from both the severity of the illness and the events that occur due to extenuating circumstances that cause family stress (McCubbin, 1988). Within the context of the Stress Process model, the conceptual framework guiding this study, family resources are viewed as a potential buffer between the secondary stressor, severity of epilepsy and the outcome of children's cognitive functioning.

This hypothesis was supported. Family resources significantly moderated the relationship between severity of epilepsy and cognitive functioning. In other words, the relationship between severity of epilepsy and cognitive functioning was not constant across levels of family resources. The post-hoc testing of the significant moderation

effect indicated that when children have lower levels of epilepsy severity, higher levels of cognitive functioning were reported by families with higher resources. However, when epilepsy is severe in children, higher family resources did not have as large of an impact on cognitive functioning scores. This may suggest that regardless of the level of family resources, the impact of severe epilepsy on cognitive functioning is unlikely to be moderated. There may be little opportunity for psychosocial factors such as family resources, to make a difference in children's cognitive functioning due to the biological imperatives of severe epilepsy.

The results of family resources as a moderator are consistent with other findings in the epilepsy literature. For example, there is evidence that family resources act as a moderator in relationships between children's cognitive functioning and academic achievement (Fastenau et al., 2004), temperament and internalizing/externalizing behaviour (Baum et al., 2004), and maternal depressive symptoms and child health related quality of life (HRQL) (Ferro et al., 2011).

Family Resources as captured by two subscales from the Family Inventory of Resources for Management (FIRM), Family Strengths: Mastery and Health and Extended Family Support measure the control, emotional support and cooperation of family members within the family environment as well as the help given and received from relatives. It has been stated that high scores on these subscales indicate a more organized family structure and strong support at home. On the other hand, low scores indicate a disorganized family environment and less support at home (Fastenau et al, 2004). When applied to the moderating effects in this thesis, the lower levels of epilepsy severity in children have less impact on their cognitive functioning when they live in families that have a more organized family environment and strong support at home.

It is possible that having an organized, supportive environment at home may help in the management of the child's epilepsy and assist in the child's cognitive functioning. For example, a more organized family could possibly promote medication adherence, which can contribute to better seizure control (Cockerell et al, 1997). This less severe epilepsy may be due to the structured family environment and have less of an impact on cognitive functioning. For those families with fewer resources, the burden of epilepsy

may threaten family homeostasis, which can lead to family dysfunction (Wood, 1993). In other research, involving parents and families in the learning process has been shown to have effects on the child's academic achievement (Christenson & Buerkle, 1999; Fish, 1995; Tizard, Schofield & Hewison, 1982).

Another potential explanation for the finding that family resources at the 12-month follow-up moderated the relationship between severity of epilepsy at 6-months and cognitive functioning at two years post diagnosis might be offered by the Convoy model presented by Kahn and Antonucci (1980). The Convoy model offers a framework to understand how an assembly of family and friends are available as resources to individuals in times of need. Life change can bring the potential to reconstruct the convoy as the individual seeks to build a network of resources that meets his/her support needs (Levitt, 2005). In the current study, this may be the mechanism whereby family resources are mobilized within a family trying to cope with epilepsy in a child acting to moderate the impact that at least less severe epilepsy has on cognitive functioning.

5.1.3 Objective 2(b) and (c) – Family Functioning and Family Demands as Mediators

Objectives 2(b) and (c) examined the potential mediating effects of family demands and family functioning on the relationship between severity of epilepsy and parent-perceived cognitive functioning. It was hypothesized that family demands would mediate the relationship between severity of epilepsy and cognitive functioning, such that families of children with severe epilepsy would endure more demands, which could result in poorer cognitive outcomes in children. It was also hypothesized that family functioning would mediate the relationship between severity of epilepsy and cognitive functioning. That is, with severe epilepsy in a child, families may experience poorer family functioning, and this could result in poorer cognitive outcomes. The rationale behind this hypothesis was that clinical aspects of epilepsy such as higher frequency of seizures, recent epilepsy diagnosis, and shorter time since last seizure were associated with high impact on families, including parent-child and marital relationships, family activities, family stress, and the level of support received (Austin & Caplan, 2007; Camfield, Breau & Camfield, 2001; Datta et al., 2006; Mims, 1997). In the few studies

that have examined the relationship between family factors and cognitive functioning, family variables such as parenting (Oostrom et al., 2003), family stress (Jones et al., 2010), and family competence (McCagh, 2009) were found to be significantly associated with cognitive functioning in children.

The mediation hypothesis was not supported in our findings, however. There are several potential explanations for why family demands and family functioning as assessed here did not show significant mediating effects. One possibility is that most of the children were reported by their paediatric neurologist as having relatively mild epilepsy, rated as not at all or a little severe on the GASE measure. This is consistent with previous literature on childhood epilepsy for the age group included in this sample (Berg et al., 1999; Cavazzuti, 1980; Eriksson & Koivikko, 1997). Such mild epilepsy may not have that large of an impact on family demands or family functioning in this sample. Also, families in this study had relatively few demands and relatively high functioning. A large percentage of families (88%) had APGAR scores over the mid-point (a score of 10), which has been suggested in the literature to differentiate between functional and dysfunctional families. Also, as indicated by the attrition analysis presented in Table 1, families who were lost to follow-up had more family demands than those families who completed the follow-up time-points. Finally, children were reported to have generally good cognitive functioning on the QOLCE subscale with a mean score of 69 (20.6). The lack of variation in family demands and family functioning, as well as for severity of epilepsy may have made it difficult to detect a mediating effect. Due to truncated variation in these variables of primary interest, the associations may have been attenuated.

5.2 Strengths

This study had multiple strengths. One advantage to this study is that the study producing the data used is longitudinal in design. The study design made it possible to observe the exposure prior to the outcome. Establishing temporality is a requirement for determining causal relationships in epidemiological research.

Second, the sample was relatively large with 374 families recruited initially and 75.7% retained across all four data collection points, which made it possible to have a large sample to perform statistical analysis of mediation and moderation.

Third, the study recruited new-onset cases making it an incidence sample rather than a prevalence sample. This is crucial as this timeframe can aid interventions for children with epilepsy who have cognitive impairments. This is a window of opportunity during which effective intervention may lessen the long-term cognitive burden of epilepsy (Loring et al., 2009).

5.3 Limitations

There are also some limitations that are important to note. The outcome variable, cognitive functioning was assessed by parent-report and is therefore a measure of parents' perceptions of their child's cognitive functioning. This measure was used because it was a more comprehensive measure of cognitive functioning assessing multiple domains as opposed to the one-item measure provided by the paediatric neurologist stating whether or not the child had cognitive impairments. The use of formal neuropsychological testing, while clearly a more rigorous method, is not often a feasible option for research studies. Although parent reports may not be optimal, one can argue that parents observe their children on a daily basis and converse with their children as well as interact with teachers, so they are likely to have a good understanding of their child's cognitive abilities. The instructions for completing the cognitive functioning subscale explain that parents should compare their child to other children of his/her own age, aimed at giving parents a perspective on their children's functioning relative to others. An exploratory/confirmatory factor analysis was completed in a separate study using the same HERQULES dataset analyzed in this thesis to assess the constructs measured by the Quality of Life in Childhood Epilepsy (QOLCE) scale. These data (unpublished) revealed that the cognitive subscale on the QOLCE, which was used as the outcome variable in this thesis, was psychometrically sound. The items from the four domains comprising the cognitive functioning subscale did not load on the other factors containing items from the subscales assessing social and behavioural outcomes. Also, none of the items comprising the cognitive

functioning subscale needed to be removed. However, when interpreting these conclusions, one must take into account that it is based on parent's report of their child's cognitive functioning.

Finally, the results for this sample of children 4-12 years of age may not be generalizable to younger or older children. However, samples that include adolescents up to 16 years of age have found similar results for the relationship between severity of epilepsy and cognitive functioning (Berg et al., 2008; Nolan et al., 2003; Schouten et al., 2002).

5.4 Recommendations for Future Research

This study demonstrated an association between severity of epilepsy and parent-perceived cognitive functioning in children with new-onset epilepsy. The relationship between severity of epilepsy and cognitive functioning was moderated by family resources; however family demands and family functioning did not significantly mediate this relationship.

More research should be done to determine whether the results of the moderating effects of family resources can be replicated. Also, when replicating results found in this thesis, a proper neuropsychological test measure should be utilized to assess the child's cognitive functioning. As this is the first study to examine the moderating effects on the relationship between severity of epilepsy and cognitive functioning, more research should be done. If the results are replicated, it is important to evaluate interventions designed to enhance family resources, as it may be an important factor in the context of paediatric epilepsy.

The findings in this thesis as well as other research indicate the importance of family factors in potentially alleviating the burden of epilepsy on both the child and family. It is important to pursue a line of research that focuses on family-centered care (FCC). Family-centred care is guided by four concepts: that health care professionals honour family perspectives and choices, information sharing between patient, family and physicians is present in order to effectively participate in care and decision-making, and that participation by family and patient is encouraged and lastly, families collaborate

with health-care professionals to develop and implement policies and programs. Children with chronic illnesses (such as neurological disabilities) are seen often by health care professionals and the complexities of their long-term needs are best addressed by FCC (King et al, 2004). Several benefits to the FCC approach have been documented. Child health outcomes such as physical, emotional, social and cognitive functioning can be positively affected by FCC (King et al, 2004). Not only does the child benefit from this care but much of the research on quality of care has focused on parental satisfaction with care, reduced stress and worry and adherence to therapy programs (King et al, 1996; Law et al, 1998; Epstein et al, 1989). The goal of health care professionals should be delivering family-centred care to enhance not only the child's quality of life (QOL) and child health outcomes, but the quality of life for all family members (Fewell & Vadasy, 1987). It is feasible that integrating the practice of FCC into the management of childhood epilepsy could improve health-care professionals' level of understanding of the available resources, extent of family demands and level of family function that characterize the families of the children they treat. This could, in turn, help to identify those families who might benefit from programs aimed at strengthening their capacity to positively influence their children's outcomes. For example, it may be possible to assist families experiencing little social support through counseling to mobilize some untapped sources of informal support available to them or to access more formal supports available through local Epilepsy Support Centres.

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Appendices

Appendix A: Strategy for Literature Search

The objective of our search strategy was to identify all published literature on the relationships examined in this thesis. We used standard search strategies involving three online databases (Medline-OVID, Pub-Med and Scopus) using keywords identified in the charts below. MESH terms were identified to ensure a thorough search within the databases. After identifying relevant articles, the ancestry method was used which evaluates the bibliographies of the collected articles.

Key words that were used are presented below. Each keyword and MESH terms of that key word were searched separately (1 through 4 in each chart), then separate key words were combined (5 through 7 in each chart).

1. Severity of epilepsy and cognitive functioning:

1. (child or adolescents).
2. (epilepsy or childhood epilepsy).
3. (cognition or cognition disorders or neuropsychological tests).
4. (seizures or epilepsy).
5. 1 and 2
6. 3 and 4
7. 5 and 6

2. Severity of epilepsy and family factors:

1. (epilepsy or childhood epilepsy).
2. (child or adolescents).
3. (stress, psychological or family or life change events).
4. (seizures or epilepsy).
5. 1 and 2
6. 3 and 4
7. 5 and 6

3. Family factors and cognitive functioning:

1. (child or adolescents).
2. (epilepsy or childhood epilepsy).
3. (stress, psychological or family or life change events).
4. cognition or cognition disorders or neuropsychological tests).
5. 1 and 2
6. 3 and 4
7. 5 and 6

Appendix B: Ethic Approval Notice

Office of Research Ethics

The University of Western Ontario

Western

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. K.N. Speechley
Review Number: 10069E
Revision Number:
Protocol Title: Health-Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes
Department and Institution: Paediatrics, Children's Hospital of Western Ontario
Sponsor: CIHR
Approval Date: 18-Nov-03
End Date: 31-Mar-06
Documents Reviewed and Approved: UWO Protocol, Letters of Information & Consent

Documents Received for Information:

This is to notify you that the University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has received and granted expedited approval to the above named research study on the date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

This approval shall remain valid until end date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;

b) all adverse and unexpected experiences or events that are both serious and unexpected;

c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interset, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

Chair of HSREB (Expedited): Dr. Paul Harding

Karen Kueneman, BA (Hons), Ethics Officer HSREB (Expedited)

Faxed (Y)N
Date: Nov 21/03

This is an official document. Please retain the original in your files.

Appendix C: Physician Form

Q___ ___ Months

PHYSICIAN FORM

Study ID __ __ __ __

Health Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes

Patient's Date of Birth (dd/mm/yy): _____ Site #:_____

Please answer the following questions based on information from this patient's most recent visit and return upon completion

1. Date of patient's last visit (dd/mm/yy): _____ or Date of Telephone F/U (dd/mm/yy)_____
2. Date form completed (dd/mm/yy): _____

If information for 3 thru 7 is unchanged from baseline (diagnosis) visit, please check here and proceed to 8. ☐

3. Seizure type(s): 1) _____ 2)_____
   3)_____ 4)_____
4. Epilepsy syndrome: _____
5. Convulsive status epilepticus:
   ☐ No
   ☐ Yes
6. Exclusive nocturnal seizures:
   ☐ No
   ☐ Yes
7. Age of first seizure (excluding febrile seizure): _____ yrs
8. Does this patient have any family with epilepsy?
   ☐ No
   ☐ Yes
9. Number of AEDs currently: _____
10. Number of AEDs total: _____
11. Is this patient of school age?
    ☐ No
    ☐ Yes → Grade: ___ ☐ regular class ☐ regular class with resource ☐ special class

PLEASE TURN OVER TO COMPLETE

12. Does the patient have behavioural problems?
☐ No (normal)
☐ Yes → Please check one: ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

13. Does the patient have cognitive problems?
☐ No (normal)
☐ Yes → Please check one: ☐ borderline ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

14. Does this patient have motor problems?
☐ No
☐ Yes → Please check one: ☐ mild ☐ moderate ☐ severe

Diagnosis: _____

15. Other neurological deficits? Please specify: _____

_____

16. Taking into account all aspects of this patient's epilepsy, how would you rate its severity at his/her last visit? Please check <u>one</u> answer.

☐ Extremely severe
☐ Very severe
☐ Quite severe
☐ Moderately severe
☐ Somewhat severe
☐ A little severe
☐ Not at all severe

17. Rate the following aspects of this patient's epilepsy at his/her last visit.

Check <u>one box</u> using the following 7-point scale:
1 = none or never
7 = extremely frequent, severe or high

	1	2	3	4	5	6	7
Frequency of seizures							
Intensity of seizures							
Falls or injuries during seizures							
Severity of post-ictal period							
Amount of antiepileptic drugs							
Side effects of antiepileptic drugs							
Interference of epilepsy or drugs with daily activities							

PLEASE FAX to: 519-685-8082

Appendix D: HERQULES Parent Questionnaire

Child Health
Research Institute

HERQULES STUDY

Health Related Quality of Life in Children with Epilepsy: The First Two Years After Diagnosis Through Parents' Eyes

Parents' Questionnaire

Q1

Throughout this questionnaire when we refer to "your child", we are referring to your child with the initials ____ ____ . Please keep this child in mind when responding to the questions.

Children's Hospital
of Western Ontario
London Health Sciences Centre

Schulich
MEDICINE & DENTISTRY

Western

Q1

Study ID __ __ __ __

I have received $5.00 as a token of appreciation for my participation in the HERQULES Study with Dr. Kathy Nixon Speechley in London Ontario.

Date: _____ Initial: _____

INSTRUCTIONS

1. **Most of the questions in this booklet ask about your child's health and well-being. A few of the questions ask about your own health and well-being. Your individual answers will remain strictly confidential.**

2. **Answer questions by checking the appropriate box (☐ Yes ☐ No ☐ Don't know) or circling the appropriate number.**

3. **Certain questions may look alike but each one is different. Some questions may ask about problems that your child does not have. Please try to answer each question as it is important for us to know when your child does not have these problems.**

4. **There are no right or wrong answers. If you are unsure how to answer a question, please give the best answer you can. Write any comments you may have on the page beside the question.**

SECTION 1:

YOUR CHILD'S PHYSICAL ACTIVITIES

The following questions ask about physical activities your child might do.

1.1. In his/her daily activities during the past 4 weeks, how often has your child:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. needed more supervision than other children his/her age?	☐	☐	☐	☐	☐	☐
b. needed special precautions (i.e. wearing a helmet)?	☐	☐	☐	☐	☐	☐
c. played freely in the house like other children his/her age?	☐	☐	☐	☐	☐	☐
d. played freely outside the house like other children his/her age?	☐	☐	☐	☐	☐	☐
e. gone swimming? (i.e. swam independently)	☐	☐	☐	☐	☐	☐
f. participated in sports activities (other than swimming)?	☐	☐	☐	☐	☐	☐
g. stayed out overnight (with friends or family)?	☐	☐	☐	☐	☐	☐
h. played with friends away from you or your home?	☐	☐	☐	☐	☐	☐
i. gone to parties without you or without supervision?	☐	☐	☐	☐	☐	☐
j. been able to do the physical activities other children his/her age do?	☐	☐	☐	☐	☐	☐

1.2. During the past 4 weeks, how much of the time do you think your child:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	Not applicable
a. felt tired	☐	☐	☐	☐	☐	☐
b. felt energetic	☐	☐	☐	☐	☐	☐

1.3. Is there anything else you would like to tell us about your child's activities?

WELL-BEING

Below is a list that describes how your child might feel in general.

1.4. During the past 4 weeks, how much of the time do you think your child:

	All of the time	Most of the time	Some of the time	A little of the time	None of the time	Not applicable
a. felt down or depressed?	☐	☐	☐	☐	☐	☐
b. felt calm?	☐	☐	☐	☐	☐	☐
c. felt helpless in situations?	☐	☐	☐	☐	☐	☐
d. felt happy?	☐	☐	☐	☐	☐	☐
e. wished s/he was dead?	☐	☐	☐	☐	☐	☐
f. felt in control?	☐	☐	☐	☐	☐	☐
g. felt tense and anxious?	☐	☐	☐	☐	☐	☐
h. felt frustrated?	☐	☐	☐	☐	☐	☐
i. felt overwhelmed by events?	☐	☐	☐	☐	☐	☐
j. worried a lot?	☐	☐	☐	☐	☐	☐
k. felt confident?	☐	☐	☐	☐	☐	☐
l. felt excited or interested in something?	☐	☐	☐	☐	☐	☐
m. felt pleased about achieving something?	☐	☐	☐	☐	☐	☐
n. got easily embarrassed?	☐	☐	☐	☐	☐	☐
o. felt different or singled out?	☐	☐	☐	☐	☐	☐
p. felt nobody understood him/her?	☐	☐	☐	☐	☐	☐
q. felt valued?	☐	☐	☐	☐	☐	☐
r. felt s/he was not good at anything?	☐	☐	☐	☐	☐	☐
s. felt no one cared?	☐	☐	☐	☐	☐	☐

1.5. Is there anything else you would like to tell us about how your child feels in general?

COGNITION

The following questions ask about some problems children have with concentrating, remembering, and speaking.

1.6. Compared to other children of his/her own age, how often during the past 4 weeks has your child:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. had difficulty attending to an activity?	☐	☐	☐	☐	☐	☐
b. had difficulty reasoning or solving problems?	☐	☐	☐	☐	☐	☐
c. had difficulty making plans or decisions?	☐	☐	☐	☐	☐	☐
d. had difficulty keeping track of conversations?	☐	☐	☐	☐	☐	☐
e. had trouble concentrating on a task?	☐	☐	☐	☐	☐	☐
f. had difficulty concentrating on reading?	☐	☐	☐	☐	☐	☐
g. had difficulty doing one thing at a time?	☐	☐	☐	☐	☐	☐
h. reacted slowly to things being said & done?	☐	☐	☐	☐	☐	☐
i. completed activities that needed organising/planning?	☐	☐	☐	☐	☐	☐
j. found it hard remembering things?	☐	☐	☐	☐	☐	☐
k. had trouble remembering names of people?	☐	☐	☐	☐	☐	☐
l. had trouble remembering where s/he put things?	☐	☐	☐	☐	☐	☐
m. had trouble remembering things people told him/her?	☐	☐	☐	☐	☐	☐
n. had trouble remembering things s/he read hours or days before?	☐	☐	☐	☐	☐	☐
o. planned to do something then forgot?	☐	☐	☐	☐	☐	☐
p. had trouble finding the correct words?	☐	☐	☐	☐	☐	☐
q. had trouble understanding or following what others were saying?	☐	☐	☐	☐	☐	☐
r. had trouble understanding directions?	☐	☐	☐	☐	☐	☐
s. had difficulty following simple instructions?	☐	☐	☐	☐	☐	☐
t. had difficulty following complex instructions?	☐	☐	☐	☐	☐	☐
u. had trouble understanding what s/he read?	☐	☐	☐	☐	☐	☐
v. had trouble writing?	☐	☐	☐	☐	☐	☐
w. had trouble talking?	☐	☐	☐	☐	☐	☐

1.7. Is there anything else you would like to tell us about your child's concentration, memory or speech?

YOUR CHILD'S SOCIAL ACTIVITIES

1.8. During the past 4 weeks, how often has your child's epilepsy:

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. limited his/her social activities (visiting friends, close relatives, or neighbours)?	☐	☐	☐	☐	☐	☐
b. helped him/her to make friends?	☐	☐	☐	☐	☐	☐
c. affected his/her social interactions at school or work?	☐	☐	☐	☐	☐	☐
d. improved his/her friendships & relationships with others?	☐	☐	☐	☐	☐	☐
e. limited his/her leisure activities (hobbies or interests)?	☐	☐	☐	☐	☐	☐
f. isolated him/her from others?	☐	☐	☐	☐	☐	☐
g. improved his/her relations with family members?	☐	☐	☐	☐	☐	☐
h. made it difficult for him/her to keep friends?	☐	☐	☐	☐	☐	☐
i. frightened other people?	☐	☐	☐	☐	☐	☐

1.9. During the past 4 weeks, how limited are your child's social activities compared with others his/her age because of his/her epilepsy or epilepsy-related problems?

☐	☐	☐	☐	☐
Yes, limited a lot	Yes, limited some	Yes, limited a little	Yes, but rarely	No, not limited

1.10. During the past 4 weeks, how often has your child freely discussed his/her epilepsy with friends?

☐	☐	☐	☐	☐
Very often	Fairly often	Sometimes	Almost Never	Not applicable

1.11. During the past 4 weeks, how often has your child freely discussed his/her epilepsy with family?

☐	☐	☐	☐	☐
Very often	Fairly often	Sometimes	Almost Never	Not applicable

1.12. Is there anything else you would like to tell us about your child's social activities?

YOUR CHILD'S BEHAVIOUR

Below are statements that describe some children's behaviour.
Please try to answer all questions as well as you can, even if some do not seem to apply to your child.

1.13. Compared to other children his/her own age, how often during the past 4 weeks do each of the following statements describe your child?

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
a. relied on you/family to do things for him/her that s/he was able to do him/herself	☐	☐	☐	☐	☐	☐
b. asked for reassurance	☐	☐	☐	☐	☐	☐
c. was socially inappropriate (said or did something out of place in a social situation)	☐	☐	☐	☐	☐	☐
d. wanted things to be perfect	☐	☐	☐	☐	☐	☐
e. did not give up easily	☐	☐	☐	☐	☐	☐
f. angered easily	☐	☐	☐	☐	☐	☐
g. hit or attacked people	☐	☐	☐	☐	☐	☐
h. swore in public	☐	☐	☐	☐	☐	☐
i. joined in activities with other children	☐	☐	☐	☐	☐	☐
j. feared unfamiliar places, situations or people	☐	☐	☐	☐	☐	☐
k. preferred his/her own company instead of seeking out others	☐	☐	☐	☐	☐	☐
l. was obedient	☐	☐	☐	☐	☐	☐
m. set high standards for self	☐	☐	☐	☐	☐	☐
n. did not worry about what others thought	☐	☐	☐	☐	☐	☐
o. get along with other children	☐	☐	☐	☐	☐	☐
p. wished s/he was someone or somewhere else	☐	☐	☐	☐	☐	☐
q. acted without thinking	☐	☐	☐	☐	☐	☐
r. demanded a lot of attention	☐	☐	☐	☐	☐	☐

Compared to other children his/her own age, how often during the past 4 weeks do each of the following statements describe your child?

	Very Often	Fairly Often	Some-times	Almost Never	Never	Not applicable
s. was decisive	☐	☐	☐	☐	☐	☐
t. was independent	☐	☐	☐	☐	☐	☐
u. preferred routines or disliked changes	☐	☐	☐	☐	☐	☐
v. did things just to prove s/he could	☐	☐	☐	☐	☐	☐
w. preferred the company of adults	☐	☐	☐	☐	☐	☐

1.14. Is there anything else you would like to tell us about your child's behaviour?

GENERAL HEALTH

1.15. Compared to other children his/her age, how do you think your child's health has been in the past 4 weeks? Please consider your child's epilepsy as part of his/her health when you answer this question.

☐ Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor

1.16. Is there anything else you would like to tell us about how epilepsy has affected your child's health?

QUALITY OF LIFE

1.17. In the past 4 weeks what has your child's quality of life been?

☐ Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor

1.18. Consider your child's present skills in thinking, learning, remembering, speaking and understanding. Taken together, do you think that your child is functioning:

- ☐ At the level expected for his/her age?
- ☐ Somewhat behind the level expected for his/her age?
- ☐ Significantly behind the level expected for his/her age?

SECTION 2:

2.1 The next questions ask about your interaction with your child's neurologist. Please think about your child's most recent visit to his/her neurologist for epilepsy care and circle the response that best represents your opinion.

a. To what extent was your child's main problem(s) discussed at that visit?

Completely Mostly A little Not at all

b. Would you say that your doctor knew that this was one of your reasons for coming in for that visit?

Yes Probably Unsure No

c. To what extent did the doctor understand the importance of your reason for coming in for that visit?

Completely Mostly A little Not at all

d. How well do you think your doctor understood you at that visit?

Very well Well Somewhat Not at all

e. How satisfied were you with the discussion of your child's problem?

Very satisfied Satisfied Somewhat satisfied Not satisfied

f. To what extent did the doctor explain this problem to you?

Completely Mostly A little Not at all

g. To what extent did you agree with the doctor's opinion about the problem?

Completely Mostly A little Not at all

h. How much opportunity did you have to ask your questions?

Very much A fair amount A little Not at all

i. To what extent did the doctor ask about your goals for your child's treatment?

Completely Mostly A little Not at all

j. To what extent did the doctor explain treatment?

Very well Well Somewhat Not at all

k. To what extent did the doctor explore how manageable this (treatment) would be for your child and you? He/she explored this:

Completely Mostly A little Not at all

l. To what extent did you and the doctor discuss your respective roles? (Who is responsible for making decisions and who is responsible for what aspects of your child's care?)

Completely Mostly A little Not at all

m. To what extent did the doctor encourage you to take the role you wanted in your child's care?

Completely Mostly A little Not at all

n. How much would you say that this doctor cares about your child as a person?

Very much A fair amount A little Not at all

SECTION 3:

3.1. The next set of questions asks about what social, psychological, community and financial resources families believe they have available to them in the management of family life. To complete this inventory you are asked to read the list of "Family Statements" one at a time. In each statement, "family" means your immediate family (mother and/or father and children.) Then ask yourself: *"How well does the statement describe our family situation?"*

Then make your decision by circling one of the following:

0 = Not At All	This statement does not describe our family situation. This does not happen in our family.
1 = Minimally	This statement describes our family situation only slightly. Our family may be like this once in a while.
2 = Moderately	This statement describes our family situation fairly well. Our family is like this some of the time.
3 = Very Well	This statement describes our family very accurately. Our family is like this most of the time.

Please read and record your decision for each of the statements below.

Family Statements:	**Not at all**	**Minimally**	**Moderately**	**Very Well**
a. Being physically tired much of the time is a problem in our family	0	1	2	3
b. We have to nag each other to get things done	0	1	2	3
c. We do not plan too far ahead because many things turn out to be a matter of good or bad luck anyway	0	1	2	3
d. Having only one person in the family earning money is (or would be) a problem in our family	0	1	2	3
e. It seems that members of our family take each other for granted	0	1	2	3
f. Sometimes we feel we don't have enough control over the direction our lives are taking	0	1	2	3
g. Certain members of our family do all the giving, while others do all the taking	0	1	2	3
h. We seem to put off making decisions	0	1	2	3
i. Our family is under a lot of emotional stress	0	1	2	3
j. Many things seem to interfere with family members being able to share concerns	0	1	2	3
k. Most of the money decisions are made by only one person in our family	0	1	2	3
l. It seems that we have more illness (colds, flu, etc.) in our family than other people do	0	1	2	3
m. In our family some members have many responsibilities while others don't have enough	0	1	2	3
n. It is upsetting to our family when things don't work out as planned	0	1	2	3
o. Being sad or "down" is a problem in our family	0	1	2	3
p. It is hard to get family members to cooperate with each other	0	1	2	3
q. Many times we feel we have little influence over the things that happen to us	0	1	2	3
r. We have the same problems over and over – we don't seem to learn from past mistakes	0	1	2	3

Family Statements:	**Not at all**	**Minimally**	**Moderately**	**Very Well**
s. There are things at home we need to do that we don't seem to get done	0	1	2	3
t. We seem to be so involved with work and/or school activities that we don't spend enough time together as a family	0	1	2	3
u. Our relatives seem to take from us, but give little in return	0	1	2	3
v. We try to keep in touch with our relatives as much as possible	0	1	2	3
w. Our relative(s) are willing to listen to your problems	0	1	2	3
x. Our relatives do and say things that make us feel appreciated	0	1	2	3

SECTION 4:

4.1. Over their life cycle, all families experience many changes as a result of normal growth and development of members and due to external circumstances. The following list of family life changes can happen in a family at any time. Because family members are connected to each other in some way, a life change for any one member affects all the other persons in the family to some degree.

*"**FAMILY**" means a group of two or more persons living together who are related by blood, marriage or adoption. This includes persons who live with you and to whom you have a long term commitment.*

Please read each family life change and decide whether it happened to any member of your family - **including you** - during the past 12 months and check **Yes** or **No**.

Did the change happen in your family:	During the Last 12 Months **Yes**	**No**	**Score**
I. Intrafamily Strains			
a. Increase of husband/father's time away from family			46
b. Increase of wife/mother's time away from family			51
c. A member appears to have emotional problems			58
d. A member appears to depend on alcohol or drugs			66
e. Increase in conflict between husband and wife			53
f. Increase in arguments between parent(s) and child(ren)			45
g. Increase in conflict among children in the family			48
h. Increased difficulty in managing teenage child(ren)			55
i. Increased difficulty in managing school age child(ren) (6-12 yrs)			39
j. Increased difficulty in managing preschool age child(ren) (2.5-6 yrs)			36
k. Increased difficulty in managing toddler(s) (1-2.5 yrs)			36
l. Increased difficulty in managing infant(s) (0-1 yr)			35
m. Increase in the amount of "outside activities" which the children are involved in			25
n. Increased disagreement about a member's friends or activities			35

Did the change happen in your family:	During the Last 12 Months		
	Yes	**No**	**Score**
o. Increase in the number of problems or issues which don't get resolved			45
p. Increase in the number of tasks or chores which don't get done			35
q. Increased conflict with in-laws or relatives			40
II. Marital Strains			
a. Spouse/parent was separated or divorced			79
b. Spouse/parent had an "affair"			68
c. Increased difficulty in resolving issues with a "former" or separated spouse			47
d. Increased difficulty with sexual relationship between husband and wife			58
III. Pregnancy and Childbearing Strains			
a. Spouse had unwanted or difficulty pregnancy			45
b. An unmarried member became pregnant			65
c. A member had an abortion			50
d. A member gave birth to or adopted a child			50
IV. Finance and Business Strains			
a. Took out a loan or refinanced a loan to cover increased expenses			29
b. Went on welfare			55
c. Change in conditions (economic, political, weather) which hurts the family investments			41
d. Change in agriculture market, stock market, or land values which hurts family investments and/or income			43
e. A member started a new business			50
f. Purchased or built a home			41
g. A member purchased a car or other major item			19
h. Increased financial debts due to over-use of credit cards			31
i. Increased strain on family "money" for medical/dental expenses			23
j. Increased strain on family "money" for food, clothing, energy, home care			21
k. Increased strain on family "money" for child(ren)'s education			22
l. Delay in receiving child support or alimony payments			41
V. Work-Family Transitions and Strains			
a. A member changed to a new job/career			40
b. A member lost or quit a job			55
c. A member retired from work			48
d. A member started or returned to work			41
e. A member stopped working for extended period (e.g., laid off, leave of absence, strike)			51
f. Decrease in satisfaction with job/career			45
g. A member had increased difficulty with people at work			32
h. A member was promoted at work or given more responsibilities			40
i. Family moved to a new home/apartment			43
j. A child/adolescent member changed to a new school			24
VI. Illness and Family "Care" Strains			
a. Parent/spouse became seriously ill or injured			44
b. Child became seriously ill or injured			35

Did the change happen in your family:	During the Last 12 Months **Yes**	**No**	**Score**
c. Close relative or friend of the family became seriously ill			44
d. A member became physically disabled or chronically ill			73
e. Increased difficulty in managing a chronically ill or disabled member			58
f. Member or close relative was committed to an institution or nursing home			44
g. Increased responsibility to provide direct care or financial help to husband's and/or wife's parents			47
h. Experienced difficulty in arranging for satisfactory child care			40
VII. Losses			
a. A parent/spouse died			98
b. A child member died			99
c. Death of husband's or wife's parent or close relative			48
d. Close friend of the family died			47
e. Married son or daughter was separated or divorced			58
f. A member "broke up" a relationship with a close friend			35
VIII. Transitions "In and Out"			
a. A member was married			42
b. Young adult member left home			43
c. Young adult member began college (or post high school training)			28
d. A member moved back home or a new person moved into the household			42
e. A parent/spouse started school (or training program) after being away from school for a long time			38
IX. Family Legal Violations			
a. A member went to jail or juvenile detention			68
b. A member was picked up by police or arrested			57
c. A member ran away from home			61
d. A member dropped out of school or was suspended from school			38

SECTION 5:

5.1. Now we would ask that you think about the following and check the answer that best describes how you feel most of the time. Please be honest.

a) When something is bothering me, I can ask my family for help.

☐	☐	☐	☐	☐
Never	Hardly	Some of the time	Almost always	Always

b) I like the way my family talks things over and shares problems with me.

☐	☐	☐	☐	☐
Never	Hardly	Some of the time	Almost always	Always

c) I like how my family lets me try new things I want to do.

☐	☐	☐	☐	☐
Never	Hardly	Some of the time	Almost always	Always

d) I like what my family does when I feel mad, happy, or loving.

☐	☐	☐	☐	☐
Never	Hardly	Some of the time	Almost always	Always

e) I like how my family and I share time together.

☐	☐	☐	☐	☐
Never	Hardly	Some of the time	Almost always	Always

SECTION 6:

6.1. Now we'd like to ask some questions about you. Please read these sentences that say something about how people sometimes feel and circle the number of the category on this page that best indicates how often you have felt this way in the past 7 days.

0. Rarely or none of the time (less than one day)
1. Some or a little of the time (1-2 days)
2. Occasionally or a moderate amount of time (3-4 days)
3. Most or all of the time (5-7 days)

During the past seven days:

a)	I was bothered by things that usually don't bother me.	0	1	2	3
b)	I did not feel like eating; my appetite was poor.	0	1	2	3
c)	I felt that I could not shake off the blues even with help from my family or friends.	0	1	2	3
d)	I felt that I was just as good as other people.	0	1	2	3
e)	I had trouble keeping my mind on what I was doing.	0	1	2	3
f)	I felt depressed.	0	1	2	3
g)	I felt that everything I did was an effort.	0	1	2	3
h)	I felt hopeful about the future.	0	1	2	3
i)	I thought my life had been a failure.	0	1	2	3
j)	I felt fearful.	0	1	2	3
k)	My sleep was restless.	0	1	2	3
l)	I was happy.	0	1	2	3
m)	I talked less than usual.	0	1	2	3
n)	I felt lonely.	0	1	2	3
o)	People were unfriendly.	0	1	2	3
p)	I enjoyed life.	0	1	2	3
q)	I had crying spells.	0	1	2	3
r)	I felt sad.	0	1	2	3
s)	I felt that people dislike me.	0	1	2	3
t)	I could not get "going".	0	1	2	3

SECTION 7:

We would like to understand and measure the experiences of parents who have a child with epilepsy. In particular we wish to know about your perceptions of the care you have been receiving over the past year from the health care institution(s) that provide(s) services to your child for his/her epilepsy.

The care that you and your child receive from this organization may bring you into contact with many individuals. The questions on this form are grouped by who these contacts are, as described below.

PEOPLE:
refers to those individuals who work directly with you or your child. These **may include** doctors, nurses, psychologists, therapists, social workers, etc.

ORGANIZATION:
refers to all staff from the health care institution(s), whether involved directly with your child or not. In addition to health care people they **may include** support staff such as office staff, housekeepers, administrative personnel, etc.

The questions are based on what parents, like yourself, have told us about the way care is sometimes offered. We are interested in your personal thoughts and would appreciate your completing this questionnaire on your own without discussing it with anyone.

7.1. For each question, please indicate how much the event or situation happens to you. You are asked to respond by circling **one** number from 1 (Not at All) to 7 (To a Very Great Extent) that you feel best fits your experience. Please note that the zero value (0) is used only if the situation described does not apply to you.

7. To a Very Great Extent
6. To a Great Extent
5. To a Fairly Great Extent
4. To a Moderate Extent
3. To a Small Extent
2. To a Very Small Extent
1. Not at All
0. Not Applicable

Indicate how much this event or situation happens to you.

IN THE PAST YEAR TO WHAT EXTENT DO THE **PEOPLE** WHO WORK WITH YOUR CHILD	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
a. help you to feel competent as a parent?	7	6	5	4	3	2	1	0
b. provide you with written information about what your child is doing in treatment?	7	6	5	4	3	2	1	0
c. provide a caring atmosphere rather than just give you information?	7	6	5	4	3	2	1	0
d. let you choose when to receive information and the type of information you want?	7	6	5	4	3	2	1	0

IN THE PAST YEAR TO WHAT EXTENT DO THE **PEOPLE** WHO WORK WITH YOUR CHILD	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
e. look at the needs of your "whole" child (e.g., at mental, emotional, and social needs) instead of just at physical needs?	7	6	5	4	3	2	1	0
f. make sure that at least one team member is someone who works with you and your family over a long period of time?	7	6	5	4	3	2	1	0
g. fully explain treatment choices to you?	7	6	5	4	3	2	1	0
h. provide opportunities for you to make decisions about treatment?	7	6	5	4	3	2	1	0
i. provide enough time to talk so you don't feel rushed?	7	6	5	4	3	2	1	0
j. plan together so they are all working in the same direction?	7	6	5	4	3	2	1	0
k. treat you as an <u>equal</u> rather than just as the parent of a patient (e.g. by not referring to you as "Mom" or "Dad")?	7	6	5	4	3	2	1	0
l. give you information about your child that is consistent from person to person?	7	6	5	4	3	2	1	0
m. treat you as an individual rather than as a "typical parent" of a child with epilepsy?	7	6	5	4	3	2	1	0
n. provide you with written information about your child's progress?	7	6	5	4	3	2	1	0
o. tell you about the results from assessments?	7	6	5	4	3	2	1	0

IN THE PAST YEAR TO WHAT EXTENT DOES THE **ORGANIZATION** WHERE YOU RECEIVE SERVICES	To a Very Great Extent	To a Great Extent	To a Fairly Great Extent	To a Moderate Extent	To a Small Extent	To a Very Small Extent	Not at All	Not Applicable
p. give you information about the types of services offered at the organization or in your community?	7	6	5	4	3	2	1	0
q. have information available about your child's epilepsy (e.g., its causes, how it progresses, future outlook)?	7	6	5	4	3	2	1	0
r. provide opportunities for the entire family to obtain information?	7	6	5	4	3	2	1	0
s. have information available to you in various forms, such as a booklet, kit, video, etc.?	7	6	5	4	3	2	1	0
t. provide advice on how to get information or to contact other parents (e.g., organization's parent resource library)?	7	6	5	4	3	2	1	0

SECTION 8:

8.1. **In general, would you say your child's health is:** (check one box only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

The following questions ask about physical activities your child might do during a day:

8.2. **During the past 4 weeks, has your child been limited in any of the following activities due to health problems?** (check one box on each line)

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Doing things that take **a lot** of energy, such as playing soccer or running?	☐	☐	☐	☐
b. Doing things that take **some** energy, such as riding a bike or skating?	☐	☐	☐	☐
c. Ability (physically) to get around the neighbourhood, playground, or school?	☐	☐	☐	☐
d. Walking one block or climbing one flight of stairs?	☐	☐	☐	☐
e. Bending, lifting or stooping?	☐	☐	☐	☐
f. Taking care of him/herself, that is, eating, dressing, bathing or going to the toilet?	☐	☐	☐	☐

8.3. **During the past 4 weeks, has your child's school work or activities with friends been limited in any of the following ways due to EMOTIONAL difficulties or problems with his/her BEHAVIOUR?** (check one box on each line)

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Limited in the **KIND** of schoolwork or activities with friends he/she could do	☐	☐	☐	☐
b. Limited in the **AMOUNT** of time he/she could spend on schoolwork or activities with friends	☐	☐	☐	☐
c. Limited in **PERFORMING** schoolwork or activities with friends (it took extra effort)	☐	☐	☐	☐

8.4. **During the <u>past 4 weeks</u>, has your child's school work or activities with friends been limited in any of the following ways due to problems with his/her PHYSICAL health?** (check one box on each line)

	Yes, limited A lot	Yes, limited some	Yes, limited a little	No, not limited
a. Limited in the **KIND** of schoolwork or activities with friends he/she could do	☐	☐	☐	☐
b. Limited in the **AMOUNT** of time he/she could spend on schoolwork or activities with friends	☐	☐	☐	☐

8.5. **During the <u>past 4 weeks</u>, how <u>much</u> bodily pain or discomfort has your child had?** (check one box only)

☐ None ☐ Very mild ☐ Mild ☐ Moderate ☐ Severe ☐ Very severe

8.6. **During the <u>past 4 weeks</u>, how <u>often</u> has your child had bodily pain or discomfort?** (check one box only)

☐ None of the time ☐ Once or twice ☐ A few times ☐ Fairly Often ☐ Very often ☐ Every/almost every day

Below is a list of items that describe chidren's behaviour or problems they sometimes have.

8.7. **How often during the <u>past 4 weeks</u> did each of the following statements describe your child?** (check one box on each line)

	Very Often	Fairly often	Some-times	Almost Never	Never
a. Argues a lot	☐	☐	☐	☐	☐
b. Has difficulty concentrating or paying attention	☐	☐	☐	☐	☐
c. Lied or cheated	☐	☐	☐	☐	☐
d. Stole things inside or outside the home	☐	☐	☐	☐	☐
e. Had tantrums or a hot temper	☐	☐	☐	☐	☐

8.8. **Compared to other children your child's age, in general would you say his/her behaviour is**: (check one only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

The following phrases are about children's moods.

8.9. **During the past 4 weeks, <u>how much of the time</u> did your child:** (check one box on each line)

		All of the time	Most of the time	Some of the time	A little of the time	None of the time
a.	Felt like crying?	☐	☐	☐	☐	☐
b.	Felt lonely?	☐	☐	☐	☐	☐
c.	Acted nervous?	☐	☐	☐	☐	☐
d.	Acted bothered or upset?	☐	☐	☐	☐	☐
e.	Acted cheerful?	☐	☐	☐	☐	☐

The following question asks about your child's satisfaction with self, school, and others. It may be helpful if you keep in mind how other children your child's age might feel about these areas.

8.10. **During the <u>past 4 weeks</u>, how satisfied do you think your child has felt about:** (check one box on each line)

		Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
a.	His/her school ability?	☐	☐	☐	☐	☐
b.	His/her athletic ability?	☐	☐	☐	☐	☐
c.	His/her friendships?	☐	☐	☐	☐	☐
d.	His/her looks/appearance?	☐	☐	☐	☐	☐
e.	His/her life overall?	☐	☐	☐	☐	☐

The following statements are about health in general.

8.11. **How true or false is each of these statements for your child?** (check one box on each line)

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. My child seems to be less healthy than other children I know.	☐	☐	☐	☐	☐
b. My child has never been seriously ill.	☐	☐	☐	☐	☐
c. When there is something going around my child usually catches it.	☐	☐	☐	☐	☐
d. I expect my child will have a very healthy life.	☐	☐	☐	☐	☐
e. I worry more about my child's health than other parents worry about their children's health.	☐	☐	☐	☐	☐

8.12. **Compared to one year ago, how would you rate your child's health now?** (check one box only)

☐	☐	☐	☐	☐
Much better now than 1 year ago	Somewhat better now than 1 year ago	About the same now as 1 year ago	Somewhat worse now than 1 year ago	Much worse now than 1 year ago

8.13. **During the <u>past 4 weeks</u>, how MUCH emotional worry or concern did each of the following cause YOU?** (check one box on each line)

	None at all	A little bit	Some	Quite a bit	A lot
a. Your child's physical health	☐	☐	☐	☐	☐
b. Your child's emotional well-being or behaviour	☐	☐	☐	☐	☐
c. Your child's attention or learning abilities	☐	☐	☐	☐	☐

8.14. **During the <u>past 4 weeks</u>, were you LIMITED in the amount of time YOU had for your own needs because of?** (check one box on each line)

	Yes, limited a lot	Yes, limited some	Yes, limited a little	No, not limited
a. Your child's physical health	☐	☐	☐	☐
b. Your child's emotional well-being or behaviour	☐	☐	☐	☐
c. Your child's attention or learning abilities	☐	☐	☐	☐

8.15. **During the past 4 weeks, <u>how often</u> has your child's <u>health or behaviour</u>:**
(check one box on each line)

	Very often	Fairly often	Some-times	Almost never	Never
a. limited the types of activities you could do as a family?	☐	☐	☐	☐	☐
b. interrupted various everyday family activities (eating meals, watching tv)?	☐	☐	☐	☐	☐
c. limited your ability as a family to "pick up and go" on a moment's notice?	☐	☐	☐	☐	☐
d. caused tension or conflict in your home?	☐	☐	☐	☐	☐
e. been a source of disagreements or arguments in your family?	☐	☐	☐	☐	☐
f. caused you to cancel or change plans (personal or work) at the last minute?	☐	☐	☐	☐	☐

8.16. **Sometimes families may have difficulty getting along with one another. They do not always agree and they may get angry. In general, how would you rate your family's ability to get along with one another?** (check one box only)

☐ Excellent ☐ Very good ☐ Good ☐ Fair ☐ Poor

These final few questions ask about your child and his/her family.

8.17. **Is your child:**

☐ Male ☐ Female

8.18. **What is your child's date of birth?**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

8.19. **Who lives with your child currently?**

Person	Their relationship to your child	Their Age	Their sex
1			☐ Male ☐ Female
2			☐ Male ☐ Female
3			☐ Male ☐ Female
4			☐ Male ☐ Female
5			☐ Male ☐ Female
6			☐ Male ☐ Female
7			☐ Male ☐ Female
8			☐ Male ☐ Female

8.20. **Is anyone helping you to complete this questionnaire?**

☐ No ☐ Yes →

If yes, who is helping you:
- ☐ Your spouse/partner
- ☐ Your child
- ☐ Other

→ **If other**, please specify:

_____

8.21. **Are you:**

☐ Male ☐ Female

8.22. **What is your date of birth?**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

8.23. **Which of the following best describes your current work status?** (check one box only)

☐	☐	☐	☐	☐	☐
Not working due to my child's health	Not working for "other" reasons	Looking for work outside the home	Working full or part-time (either outside the home or at a home-based business	Full time homemaker	Student

8.24. **What is your relationship to this child?** (check one box only)

☐ Biological parent	☐ Step parent	☐ Foster parent	☐ Adoptive parent	☐ Guardian	☐ Other (please explain on the line below)

8.25. **What is the highest grade of school you have completed?**

☐ less than 8 years
☐ 8-12 years
☐ completed high school
☐ completed vocational/technical training
☐ completed college/university
☐ completed graduate school

8.26. **What is your current marital status?** (check one box only)

☐ Married	☐ Widowed	☐ Divorced	☐ Separated	☐ Remarried	☐ Never married

8.27. **Are you currently living with a spouse or partner?**

☐ Yes ☐ No → If no, go to question 8.30.

8.28. **Which of the following best describes your spouse's/partner's current work status?** (check one box only)

☐ Not working due to my child's health	☐ Not working for "other" reasons	☐ Looking for work outside the home	☐ Working full or part-time (either outside the home or at a home-based business	☐ Full time homemaker	☐ Student

8.29 **What is the highest grade of school your spouse/partner has completed?**

☐ less than 8 years
☐ 8-12 years
☐ completed high school
☐ completed vocational/technical training
☐ completed college/university
☐ completed graduate school

The next two questions will allow us to compare your family's health to that of other people in the study who are similar to you.

8.30. **In which category is your total yearly household income before taxes?**
(check one box only)

- ☐ Less than $10,000
- ☐ $10,000 - $19,999
- ☐ $20,000 - $29,999
- ☐ $30,000 - $39,999
- ☐ $40,000 - $49,999
- ☐ $50,000 - $59,999
- ☐ $60,000 - $69,999
- ☐ $70,000 - $79,999
- ☐ $80,000 - $89,999
- ☐ $90,000 - $99,999
- ☐ $100,000 or more
- ☐ Don't know

8.31. **Thinking about your total family income, from which sources did your family receive income during the past year?** (check all that apply)

- ☐ Wages and salaries
- ☐ Income from self-employment
- ☐ Family allowance (baby bonus)
- ☐ Unemployment insurance or strike pay
- ☐ Worker's compensation
- ☐ Old Age Security, Guaranteed Income Supplement, Canada or Quebec Pension Plan, Retirement Pension Plan, Super-annuation
- ☐ Dividends and interest on bonds, deposits, and saving certificates
- ☐ Other government sources such as welfare, mother's allowance, etc.
- ☐ Other sources(s), please specify: _____

8.32. **How long ago was your child *first* diagnosed with epilepsy?**

_____ Months ago or _____ Weeks ago

8.33. **Who *first* diagnosed your child with epilepsy?** (check one box only)

- ☐ Family Physician
- ☐ Neurologist
- ☐ Pediatrician
- ☐ Other (please specify) _____

8.34. **Did the doctor who first diagnosed your child with epilepsy prescribe any medications for seizures?**

- ☐ Yes
- ☐ No

8.35. **DATE THIS QUESTIONNAIRE WAS COMPLETED:**

☐☐ / ☐☐ / ☐☐
DAY MONTH YEAR

Thank you for participating in this study.

If there are any other issues concerning your child's health and quality of life that we did not ask but that you would like us to know about, please feel free to mention them below.

Curriculum Vitae

Name: Anastasia Lambrinos

Post-secondary Education and Degrees:
Wilfrid Laurier University
Brantford, Ontario, Canada
2006-2010 B.A.

The University of Western Ontario
London, Ontario, Canada
2010-2012 M.Sc.

Honours and Awards:
Wilfrid Laurier University Entrance Scholarship
2006

Children's Health Research Institute
Graduate Assistant Scholarship
2010-2012

Schulich School of Medicine and Dentistry
Graduate Scholarship
2010-2012

Related Work Experience
Teaching Assistant
Wilfrid Laurier University
2009-2010

Research Assistant
The University of Western Ontario
2010-2012

Presentations:

Anna Lambrinos, William Avison, GuangYong Zou, Mark Ferro, Kathy Nixon Speechley. Severity of Epilepsy and Cognitive Functioning in Children with Epilepsy: A Prospective Study of Family Factors as Mediators and Moderators. *Annual Meeting of American Epilepsy Society, San Diego Convention Centre, San Diego, California. November 30 2012.* (Poster presentation)

Anna Lambrinos, William Avison, GuangYong Zou, Kathy Nixon Speechley. A Longitudinal Study of the Role of Family Factors on the Relationship between Severity of Epilepsy and Cognitive Functioning in Children. *Paediatric Research Day,*

Department of Paediatrics, The University of Western Ontario, London, Ontario. May 16 2012. (Poster presentation)

Anna Lambrinos, William Avison, GuangYong Zou, Kathy Nixon Speechley. Severity of Epilepsy and Cognitive Functioning in Children with Epilepsy: A Prospective Study of Family Factors as Mediators and Moderators. *London Health Research Day, London Convention Centre, London, Ontario. March 20 2012.* (Poster presentation)