To my family
ACKNOWLEDGMENTS

I thank my husband and family for their love and support throughout this process. I am also grateful to my mentor for the excellent training he provided and his ongoing guidance.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td>4</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>7</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>8</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>9</td>
</tr>
<tr>
<td>CHAPTER</td>
<td></td>
</tr>
<tr>
<td>1 INTRODUCTION</td>
<td>11</td>
</tr>
<tr>
<td>Anti-Epileptic Medication and Weight Status</td>
<td>17</td>
</tr>
<tr>
<td>Valproate</td>
<td>17</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>18</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>18</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>19</td>
</tr>
<tr>
<td>Health Behaviors and Growth Velocity</td>
<td>20</td>
</tr>
<tr>
<td>Psychosocial Functioning and Epilepsy</td>
<td>23</td>
</tr>
<tr>
<td>Primary Aims and Hypotheses</td>
<td>25</td>
</tr>
<tr>
<td>Aim 1: To Describe Weight Status in Youth with Epilepsy Who Are Prescribed AEDs</td>
<td>25</td>
</tr>
<tr>
<td>Aim 2: To Examine the Relationship Between Behavioral Health Factors (E.G., Caloric Intake, Energy Expenditure) and Weight Status in Youth on AEDs</td>
<td>26</td>
</tr>
<tr>
<td>Aim 3: To Assess the Relationship Between Weight Status and Psychosocial Functioning in Terms of Depressive Symptoms and Quality of Life in Youth with Epilepsy</td>
<td>26</td>
</tr>
<tr>
<td>Exploratory Analyses</td>
<td>27</td>
</tr>
<tr>
<td>2 METHOD</td>
<td>29</td>
</tr>
<tr>
<td>Participants</td>
<td>29</td>
</tr>
<tr>
<td>Procedure</td>
<td>29</td>
</tr>
<tr>
<td>Measures</td>
<td>30</td>
</tr>
<tr>
<td>Questionnaires</td>
<td>30</td>
</tr>
<tr>
<td>Anthropometrics</td>
<td>33</td>
</tr>
<tr>
<td>Medical Records/Chart Review</td>
<td>33</td>
</tr>
<tr>
<td>Statistical Analyses</td>
<td>33</td>
</tr>
<tr>
<td>Sample Size</td>
<td>33</td>
</tr>
<tr>
<td>Preliminary Data Analyses</td>
<td>34</td>
</tr>
<tr>
<td>Primary Analyses</td>
<td>35</td>
</tr>
<tr>
<td>Exploratory Analyses</td>
<td>36</td>
</tr>
</tbody>
</table>
3 RESULTS ........................................................................................................................................... 37

Preliminary Analyses .................................................................................................................. 37
Aim 1 - Weight Status Between Groups ............................................................................. 40
Aim 2 - Behavioral Health Factors Between Groups ......................................................... 41
Aim 3 - Psychosocial Functioning Between Groups ......................................................... 42
Exploratory Analyses ......................................................................................................... 43

4 DISCUSSION ...................................................................................................................................... 56

Aim 1- AEDs and Weight Status ......................................................................................... 56
Behavioral Health Factors .................................................................................................. 59
  Dietary Intake ..................................................................................................................... 59
  Physical Activity ................................................................................................................. 62
Psychosocial Functioning ..................................................................................................... 64
Limitations .............................................................................................................................. 67
Summary ...................................................................................................................................... 71

APPENDIX: MEASURES ............................................................................................................. 72

  Parent Measures .................................................................................................................. 72
  Chart Review and Administrative Forms ........................................................................ 79

LIST OF REFERENCES ............................................................................................................... 83

BIOGRAPHICAL SKETCH ........................................................................................................ 91
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1</td>
<td>Hypothesized Trajectory of Growth Acceleration and Mechanisms Underlying Accelerated Weight Gain for Weight-Positive AEDs</td>
<td>28</td>
</tr>
<tr>
<td>3-1</td>
<td>Demographic Characteristics Across Participants by AED Category</td>
<td>44</td>
</tr>
<tr>
<td>3-2</td>
<td>Gender, Minority Status, and Age for All Participants Entered into the Frequency Match Procedure</td>
<td>45</td>
</tr>
<tr>
<td>3-3</td>
<td>Demographics, Epilepsy Type, Time Since Diagnosis, Seizure Frequency, Medications, and BMI Z-Scores by AED Group for Matched Sample</td>
<td>46</td>
</tr>
<tr>
<td>3-4</td>
<td>Behavioral Health Factors by AED Group for Matched Sample</td>
<td>48</td>
</tr>
<tr>
<td>3-5</td>
<td>Pearson Product Correlations Among Psychosocial and Weight Status Variables for Matched Sample</td>
<td>49</td>
</tr>
<tr>
<td>3-6</td>
<td>Psychosocial Functioning by Group for Matched Sample</td>
<td>50</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>3-1</td>
<td>Participant Flow Chart</td>
<td>51</td>
</tr>
<tr>
<td>3-2</td>
<td>Proposed Mediation of AEDs and Change in Weight Status by Average Caloric Intake</td>
<td>52</td>
</tr>
<tr>
<td>3-3</td>
<td>Proposed Mediation of AED and Change in Weight Status by Physical Activity</td>
<td>53</td>
</tr>
<tr>
<td>3-4</td>
<td>Proposed Mediation Model for AED and Depressive Symptoms by Change in Weight Status</td>
<td>54</td>
</tr>
<tr>
<td>3-5</td>
<td>Proposed Mediation Model for AED and Quality of Life by Change in Weight Status</td>
<td>55</td>
</tr>
</tbody>
</table>
EXAMINING THE CONTRIBUTION OF HEALTH BEHAVIORS AND PSYCHOSOCIAL FUNCTIONING IN ANTI-EPILEPTIC DRUG INDUCED WEIGHT GAIN AMONG CHILDREN WITH EPILEPSY

By

Katherine Wells Follansbee-Junger

August 2012

Chair: David Janicke
Major: Psychology

Anti-epileptic drugs (AEDs) are the first line of treatment in pediatric epilepsy and successfully prevent seizure recurrence in the majority of patients. However, several of these medications have been linked to increased growth velocity, which increases risk for a range of medical and psychosocial comorbidities. The pathophysiology of changing growth status is unknown, but theories include increased appetite, reduced metabolism, and increased fatigue. The purpose of the present study was to evaluate the role of dietary intake and physical activity, the behavioral proxies of appetite and fatigue, in weight status change among children taking AEDs. Depressive symptoms and quality of life were also assessed. Participants included 49 youth, ages 8-17, and their parent/legal guardian who were assessed at baseline and 4-6 month follow-up. Children on weight-positive AEDs were compared to those taking weight-negative, neutral, or no AEDs. Due to group size imbalance, frequency matching across age, race, and gender was used to select 7 cases in each group (14 participants total) to comprise the final sample for analysis. No differences emerged in weight status, dietary intake, physical activity, or depressive symptoms between groups at baseline or over
time. Those taking weight-positive AEDs had significantly lower quality of life at baseline compared to those not on weight-positive AEDs. Across all participants at baseline, there were non-significant trends between higher weight status and higher levels of depressive symptoms, and higher weight status and better quality of life. The results of this study are consistent with previous research showing that children with epilepsy are at greater risk for being overweight/obese and having a lower quality of life than the general population. Further research with larger sample sizes targeting children at diagnosis is needed to elucidate the role of dietary intake and physical activity in AED induced weight gain.
CHAPTER 1
INTRODUCTION

Epilepsy is the most common, chronic neurological disorder of childhood, with a prevalence rate of nearly 1% in children under 16 years of age (Shinnar & Pellock, 2002). It is a heterogeneous disorder with numerous etiologies including developmental brain malformations, trauma, illness, vascular defects, and metabolic disorders (Leonard & George, 1999). The International League Against Epilepsy developed a nosology for epilepsy that classifies seizures on three levels: (1) site of epileptic discharge (partial/localized, generalized, or indeterminate); (2) group of syndromes (idiopathic, symptomatic, or cryptogenic); and (3) specific syndrome (Shinnar & Pellock, 2002). Idiopathic refers to seizures associated with genetic defects and age-dependent epilepsies (i.e., benign rolanic and absence). Symptomatic includes seizures associated with brain injury, lesions, or static encephalopathy. Cryptogenic is defined as seizures occurring in the absence of identifiable pathology and with unknown etiology (Leppik, 1998). Community based studies have found that among those with childhood onset epilepsy, partial or localized seizures accounted for approximately 60% of seizures, followed by generalized (~30%) and undetermined (~10%) (Berg, Levy, Testa & Shinnar, 1999; Sillanpaa, Jalava, & Shinnar, 1999). Developmental disabilities such as mental retardation, cerebral palsy, and autism are much more common among children with epilepsy compared to children in the general population, with comorbidity rates between 30-40% (Sillanpaa, 1992). Epilepsy occurs at the highest rate among children with severe mental retardation and when co-occurring, seizure onset tends to be earlier and prognosis less favorable compared to children of normal intelligence or those with less severe intellectual deficits (Leonard & George, 1999).
Regarding the course of illness, the median age of seizure onset in children is between 5 and 6 years, (Shinnar & Pellock, 2002) while the highest incidence rate occurs in children under 1 (Pellock, 2004). After having 1 seizure, the recurrence rate is approximately 40% by 2 years (Berg & Shinnar, 1991). It has been reported that approximately 55-65% of children who experience a seizure eventually become seizure free (Holland & Glauser, 2007; Sillanpaa, Jalava, Kaleva, & Shinnar, 1998), with many achieving remission within 2 years of beginning anti-epileptic drugs (AEDs) (Berg, Shinnar, Levy, Testa, Smith, et al., 2001). Idiopathic epilepsies (such as benign rolandic and absence epilepsies), which comprise around 30% of cases in community samples, have the best prognosis followed by cryptogenic then remote symptomatic etiologies (Leppik, 1998; Shinnar & Pellock, 2002).

Berg and colleagues (2001) followed 613 children with newly diagnosed epilepsy and classified outcomes at 2 years as good (in remission for at least 1 year at the 2 year follow-up), intractable (failed 2 or more AEDs and experienced 1 or more seizures per month for more than 18 months), and indeterminate (did not meet criteria for the other categories). Results showed that 52% of patients were in remission at 2 years, while 8% were categorized as intractable, and 38% were judged to have an indeterminate outcome at that time. Importantly, children in the indeterminate group had higher rates of discontinuous treatment and episodes of non-compliance with the medical regimen compared to those in the other 2 categories. Two year outcomes were highly predictive of status at 4 years with 83% and 87% of children maintaining their classifications as in remission or intractable, respectively. In addition, 54% of children who were indeterminate at 2 years achieved remission by 4 years. Etiology was strongly
associated with remission status in that idiopathic epilepsies were the least likely and remote symptomatic etiologies the most likely to be intractable. No association was found between cryptogenic etiologies and remission status. Children with epilepsy onset before age 1 were at the greatest risk for intractability. In summary, AED medications effectively prevent seizure recurrence in the majority of children; therefore, identifying factors that may compromise treatment adherence is essential to ensure the best outcomes for children with epilepsy.

While AEDs confer clear benefits in terms of seizure reduction and disease management among children with epilepsy, it is well established that several of these medications are associated with clinically significant weight change (Biton, 2003a,b; Grosso, Mostardini, Piccini, & Balestri, 2009). Indeed, weight gain is the most frequently reported adverse side effect of the widely used medication, valproate (Biton, Mirza, Montouris, Vuong, Hammer, & Barrett, 2001; Stephen, Sills, Leach, Butler, Parker, Hitiris, et al., 2007), occurring in up to 70% of adult patients (Corman et al., 1997). In children weight gain has been reported to be slightly less prevalent, approximately affecting 45-60% of those taking the medication (Egger & Brett, 1981; Wirrell, 2003). Clinically significant weight change has generally been defined as a 5% or 5kg change in weight from baseline in adults (Biton, 2003b). In children, who are still growing, excessive weight has been measured by an increase in BMI z-score (Jallon & Picard, 2001; Novak, Maytal, Alshansky, Eviatar, Sy-Kho et al., 1999), which adjusts for expected growth based on age and gender.

AEDs have been categorized according to their typical effects on weight status including as being associated with weight gain (e.g., valproate, carbamazepine,
gabapentin, and vigabatrin), weight loss (topiramate, felbamate, and zonisimide), or as having no effect on weight (phenytoin, lamotrigine, and levetiracetam) (Biton, 2003b; Jallon & Picard, 2001; Vanina, Podolskaya, Sedky, Shahab, Siddiqui, et al., 2002). These are herein referred to as “weight positive”, “weight negative”, or “weight neutral”, respectively. The majority of studies have been conducted on valproate simply because it has been in use the longest but an increasing body of evidence is growing to evaluate other weight positive AEDs (Biton, 2003b).

Several reviews that have summarized the effects of AED on weight status (Biton, 2003b; Jallon & Picard, 2001; Vanina et al., 2002), indicate that valproate is most strongly associated with weight gain. The accelerated growth velocity attributed to valproate typically occurs within the first 3 months of AED treatment, plateaus by month 6, and remains stable for the duration of treatment (see Biton, 2003b; Zimmerman, Kraus, Himmerich, Schuldi & Pollmacher, 2003). Similar data is not available for other weight positive AEDs in part because they are newer and have been the focus of fewer investigations. Therefore, documenting the trajectory of accelerated growth for the other weight positive AEDs is an important step in this line of research.

It is not only imperative to know which AEDs cause weight gain and the course, but also to be able to preemptively identify patients at risk for experiencing inappropriate weight gain as a side effect. Predictors of accelerated growth are poorly understood and findings across studies have been inconsistent (Biton, 2003b). For instance, the relationship between baseline weight status and change in growth velocity subsequent to AED therapy has been mixed with some studies showing that weight gain tends to be most severe among patients who were normal weight status before initiation of AEDs.
(Corman et al., 1997; Jallon & Picard, 2001), and others finding the greatest increase in BMI z-score among children who were the most overweight prior to intervention (Novak et al., 1999; Wirrell, 2003). Similar inconsistencies have been documented for gender (e.g., Isojarvi, Laatikainen, Knip, Pakarinen, Juntunen, et al., 1996; Novak et al., 1999). Importantly, most studies investigating weight gain have relied on small samples, thus assessment of risk factors has been limited due to a lack of power (Biton, 2003b).

Clinically significant weight gain as a side effect of AED treatment may reduce tolerance for the medical regimen and lead to noncompliance (Egger & Brett, 1981; Zimmerman et al., 2003), consequently impeding disease management (Wirrell, 2003; Zimmerman et al., 2003), especially among adolescents who tend to have more body concerns (Biton, 2003b). Children and adolescents may elect to terminate the AED, with or without the treatment team’s knowledge, or switch to another medication despite having a positive response in terms of seizure control to avoid or reverse weight gain (Wirrell, 2003).

Besides the direct negative influence on physical health in children with epilepsy via treatment noncompliance, childhood obesity increases the risk for a range of chronic health conditions including type II diabetes, metabolic syndrome, polycystic ovaries, and other risk factors for cardiovascular disease including hypertension and hypercholesterolemia (Fagot-Campagna, Pettitt, Engelgau, Burrows, Geiss, Valdez et al. 2000; Strauss, 1999; Weiss, Dzuira, Burgert, et al., 2004). Indeed, one study conducted among 20 prepubertal girls found that valproate-induced obesity was linked to the development of insulin sensitivity after one year, which was unrelated to serum valproate or baseline weight status (Verotti, Basciani, De Simone, Trotta, Morgese, et
Another study among 16 women found that valproate-induced obesity was linked to the development of polycystic ovaries, hyperadrogenism, abnormal lipid profiles, and hyperinsulinaemia, which resolved within a year after patients were switched to lamotrigine and lost weight (Isojarvi, Rattya, Myllyla, Knip, Koivunen, et al., 1998). What is especially troubling is that AED induced weight gain could not only exacerbate these complications among previously overweight children but produce new risk in children who move from normal to overweight status as a result of treatment.

In addition, overweight children are more likely than non-overweight youth to experience impaired psychosocial functioning, such as low self-esteem (Erermis, Cetin, Tamar, Bukusoglu, Akdeniz, & Goksen, 2004; Pierce & Wardle, 1997), depression (Davison, & Birch, 2001; Must, 1996), stigmatization (Puhl, & Latner, 2007) and negative body image (Pesa, Syre, & Jones, 2000). Children with epilepsy are already at much greater risk for suffering from psychological and behavioral disorders compared to healthy peers (Batzel, Dodrill, Dubinsky, Ziegler, Connolly, Freeman, et al., 2007; Smith, M.L., Elliot, I.M., Lach, 2004), with psychiatric comorbidity rates between 30-50% (Salpekar & Dunn, 2007). Difficulties in this population include higher rates of academic problems, attention deficit/hyperactivity disorder, depression, anxiety, peer victimization, bipolar disorder, impaired self-esteem, lower self-competence, poorer communication, lower quality of life, and more disruptive behavior disorders (see Leonard & George, 1999; Pellock, 2004; Salpekar & Dunn, 2007; Shinnar & Pellock, 2002 for review). Higher rates of psychosocial difficulties have also been documented among children with epilepsy compared to other chronic illness populations, including children with asthma, diabetes (reported in Salpekar & Dunn, 2007), and juvenile rheumatoid arthritis.
In light of these data, medications which contribute to overweight among children with epilepsy may compound psychosocial dysfunction which could act as both a barrier to compliance with epilepsy treatment as well as to adopting positive lifestyle behaviors associated with maintenance of a healthy body mass index.

Anti-Epileptic Medication and Weight Status

Given that increased growth velocity resulting from AED treatment in children with epilepsy poses significant risks to both physical and mental health, delineating the mechanisms which support increased weight status is imperative and is the first step to developing an intervention to reduce weight gain as a side effect of treatment and to mitigate the associated risks. While a substantial amount of research exists documenting the relationship between AEDs and weight status (Biton, 2003b; Jallon & Picard, 2001; Vanina et al., 2002), to date there is limited understanding of the pathophysiological mechanisms to explain the propensity for accelerated growth velocity among weight-positive AEDs. Several reviews (Biton, 2003b; Jallon and Picard, 2001; Zimmerman et al., 2003) are available that summarize what is currently known about the trajectory of AED induced weight gain and hypothesized mechanisms. An overview of these findings by medication will be provided below (Table 1-1).

Valproate

Several different mechanisms have been offered to explain valproate induced weight gain including increased appetite and thirst, increased consumption of carbohydrates, increased secretion of insulin and proinsulin, decreased energy expenditure, reduced basal energy turnover, and decreased leptin (see Biton, 2003b; Jallon & Picard, 2001; Zimmerman et al., 2003). In a study conducted among 100
children and adolescents, 38% of children who had been typically developing reached the 98thile for weight gain velocity following initiation of valproate, which was explained by an increase in appetite (Egger & Brett, 1981). In the same study, lethargy was reported among 9% of youth initiating valproate. However, among the patients who suffered from lethargy, decreased appetite and weight loss were also reported, suggesting that reduction in physical activity is an unlikely explanation for weight gain, at least among children. Importantly, the data in this study was gathered through a retrospective chart review without validated measures of dietary intake and physical activity. It appears that increased appetite was merely documented by anecdotal parent and child report.

**Carbamazepine**

Little research has investigated the cause of weight gain associated with carbamazepine treatment; however, proposed mechanisms include edema due to increased secretion of antidiuretic hormones, and increased appetite and caloric intake (see Biton, 2003b; Jallon & Picard, 2001). Very little research has been conducted among children and trajectory of growth velocity change has not been documented.

**Vigabatrin**

Controlled clinical trials examining the tolerability and efficacy of vigabatrin have suggested a dose-dependent relationship between the medication and weight gain reported as a side effect (see Biton, 2003b). An explanatory mechanism has not yet been offered (Biton, 2003b; Jallon & Picard, 2001) and description of the growth trajectory has not been reported.
Gabapentin

No research has examined mechanisms causing weight gain for this drug; however, increased consumption of carbohydrates and reductions in energy expenditure have been documented for other GABAergic drugs (see Biton, 2003b). Again, the course of change in weight status subsequent to gabapentin is unknown.

In summary, data examining the pathogenesis of AED induced weight gain is preliminary and wrought with limitations. Specifically, many of the studies cited in these reviews relied on cross-sectional or retrospective data, chart reviews, small sample sizes, non-randomized designs, and clinical anecdotes (Biton, 2003b). While these types of studies are important for generating hypotheses they cannot be used as evidence to support causal statements about the mechanisms underlying change.

Furthermore, very few studies were conducted with the express purpose of investigating AED induced weight gain. In drug studies assessing tolerability and efficacy of medications, weight gain was often tracked only as an adverse side effect. This is problematic not only because data to assess proposed mechanisms of accelerated weight gain (e.g., assessment of metabolic parameters, dietary intake, energy expenditure, appetite) were not included but also because the incidence of excessive weight gain may be underreported as an adverse side effect. In one trial of valproate and carbamazepine, excessive growth velocity as determined by exceeding the 97th centile for age and gender was documented in 26% and 29% of children, respectively. However, it was only reported as an adverse side effect by 9% of the patients on valproate and 4% of the patients on carbamazepine (Easter, O'Bryan-Tear, & Verity; 1997). The true incidence of AED induced weight gain can only be determined by using objective measures of height and weight over time.
This gap in knowledge is especially pronounced for the newer medications vigabatrin and gabapentin, and among children who have been the focus of far fewer studies. So far, investigations of vigabatrin and gabapentin have mostly utilized add-on designs (i.e., adding the new AED to an existing regimen); thus, findings are confounded by potential interactions related to polytherapy (Biton, 2003b). Properties of medications with similar mechanisms of action have also been extrapolated to the newer AEDs without evaluation of those properties in the AED of interest. In children retrospective chart reviews have commonly been used to examine the relationship between measures height and weight and medications over time (e.g., Egger & Brett, 1981; Wirrell, 2003). This provides documentation of the relationship between AED and weight status change but offers little by way of explaining of the mechanisms involved.

**Health Behaviors and Growth Velocity**

To expand on existing knowledge and contribute to the growing body of research evaluating AED induced weight gain, the proposed mechanisms listed above could be evaluated to some extent by assessing for changes in measurable health behaviors. On a basic level, weight gain results from a positive imbalance between energy intake and energy expenditure, which in terms of behavior is regulated by caloric intake and physical activity. The pathophysiology underlying increased growth velocity should manifest in detectable patterns in energy regulating behaviors, such that alterations in these behaviors subsequent to AED therapy may reveal the source of the energy imbalance. For instance, if the mechanism catalyzing weight gain is appetite stimulation (Luef, Abraham, Haslinger, Trinka, Seppi et al., 2002), then increases in caloric intake subsequent to initiation of AED should be observed. Some have proposed an increase in specific nutrients such as carbohydrates and sweets (see Zimmerman et al., 2003),
which could be also be evaluated through the prospective assessment of dietary intake. On the other hand, increasing growth velocity despite stable caloric intake and physical activity could indicate depressed metabolism or a reduction in basal energy turnover as the culprit (Leibowitz, 1992; Zimmerman et al., 2003). Beyond providing data to support or dispute existing hypotheses about the source of accelerated weight gain in children on AEDs, delineating the role of modifiable health behaviors may provide a concrete target for clinical intervention. Children and families could be taught preventative strategies such as monitoring, meal planning, increasing fruit and vegetable intake, and problem-solving techniques (Epstein, Paluch, Roemmich, & Beecher, 2007; Janicke, Sallinen, Perri Lutes, Huerta, Silverstein, & Brumback, 2008) to reduce weight gain as a side effect of treatment, with corresponding benefits in terms of treatment compliance, seizure reduction, and preclusion of obesity-related physical and psychosocial complications.

Physical activity plays an important role in maintaining a healthy weight status among children and is the only manipulatable variable influencing energy expenditure (Spear, Barlow, Ervin, Ludwig, Saelens, Schetzina, & Taveras, 2007). Research suggests that overweight children take approximately 3000 less steps per day than their normal weight peers (Tudor-Locke, Williams, Reis, & Pluto, 2002), and increasing physical activity among overweight children is frequently a component of weight management programs designed to improve children’s weight status (Janicke et al., 2008; Wilfley, Tibbs, Van Buren, Reach, Walker, & Epstein, 2007). Increased levels of physical activity have been associated with lower cardiovascular risk factors, BMI, and body fat, as well as improved maintenance of healthy body weight (see Spear et al.,
Previous studies investigating the impact of epilepsy on quality of life have indicated that children diagnosed with epilepsy have restricted access to physical activities (Van Empelen, Jennekens-Schinkel, van Rijen, Holders, & van Nieuwenhuizen, 2005), compared to healthy peers or siblings, such as less time spent participating in organized athletics and extracurricular activities (Arida, Cavalheiro, de Silva, & Scorza., 2008; Wong & Wirrell, 2006). Individuals with epilepsy as well as their physicians and caretakers often harbor concerns that engaging in physical activity will cause seizures (Ablah, Haug, Konda, Tinius, Ram, Sadler, & Liow, 2009). The physical toll of inactivity in this population has been documented: compared to those in general population, people with epilepsy display lower levels of muscle strength, flexibility (Steinhoff, Neususs, Thegeder, & Reimers, 1996), endurance (Bjorholt, Nakken, Rohme, & Hansen, 1990) and maximum oxygen intake (Nakken, Bjorholt, Johannessen, Loyning, & Lind, 1990). On the contrary, emerging data suggests that physical activity may not only facilitate cardiovascular and emotional health (Ericksen, H.R., Ellertsen, B., Gronningsaeter, H., Nakkan, K.O., Loyning, Y., & Ursin, H., 1994), but it may actually reduce seizure frequency in those with epilepsy (Arida et al., 2008; Eriksen et al., 1994). Reduction of seizure frequency as a result of AEDs may offer affected youth new opportunities to become more active (Elliot, Lach, & Smith, 2000). Indeed, the American Academy of Pediatrics (1983) released a position statement acknowledging the importance of athletic endeavors in children and adolescents and stated that participation in such activities should not be restricted when seizure control is good with the exception of activities that could reasonably result in head injuries or injury. The International League Against Epilepsy later advised that the only activities
that sports that should be prohibited in epilepsy are sky diving and scuba diving (Commission of Pediatrics of the International League of Epilepsy, 1997). Thus, it is important to consider physical activity in health promotion among children with epilepsy.

The studies described above that reported on rates of physical activity in individuals with epilepsy typically utilized self-report and questionnaire data, which can be unreliable especially when assessing behaviors over extended periods of time and among younger children. Objective documentation of physical activity patterns in children on AED medications could provide important information about activity patterns, the influence of AEDs on activity levels, and help to explore whether individuals who achieve good seizure control are in fact able to embrace opportunities to become more active.

**Psychosocial Functioning and Epilepsy**

As stated above, an abundance of literature has documented higher rates of psychopathology among children with epilepsy (e.g., Leonard & George, 1999; Pellock, 2004; Salpekar & Dunn, 2007) and overweight children (e.g., Eremis et al., 2004; Zeller & Modi, 2008) individually compared to healthy peers, however no research has explicitly investigated the effect of overweight on psychosocial functioning among children with epilepsy. Children with epilepsy are at greater risk for psychosocial dysfunction than any other chronic illness population (Rutter, Graham, & Yule, 1970), with comorbidity rates reported to be between 30-60% (Salpekar & Dunn, 2007). Approximately 1 in 4 children with epilepsy report clinically significant depression, which presents a particular threat in this population due to the higher rates of suicide compared to children without epilepsy (Plioplys, 2003). Higher levels of depressive symptomatology (Eremis et al., 2004), suicidal ideation, and suicide attempts (see Puhl
Both children with epilepsy and overweight children also report impaired quality of life compared to healthy peers. Epilepsy is accompanied by a wide range of psychosocial stressors for the affected child and their family, including missed days at work and school, loss of control and unpredictable seizures, restrictions on reaching developmental milestones such as driving and achieving autonomy, family discord, financial burden, cognitive impairment, and stigmatization (Leonard & George, 1999; Salpekar & Dunn, 2007). These factors interact to reduce functioning across multiple domains including physical, social, and cognitive quality of life (Van Empelen et al., 2005). Similarly, one study comparing overweight to non-overweight children and adolescents found that overweight youth reported significantly worse quality of life at a level comparable to children undergoing chemotherapy (Schwimmer, Burwinkle, & Varni, 2003).

Understanding the impact of AED induced weight gain among children with epilepsy in terms of depressive symptoms and quality of life is therefore imperative to evaluate the clinical significance of overlapping risk. It is possible that both having epilepsy and being overweight exacerbate risk for psychopathology in terms of prevalence, severity, course, and prognosis. In addition, impaired emotional and social functioning may interfere with children’s ability to adopt a more active lifestyle (Smith et al., 2004) and impede successful weight management. Separate bodies of literature underscore the importance of early detection and intervention for psychiatric comorbidities in each of these populations (e.g., Leonard & George, 1999; Puhl &
Latner, 2007) yet until it is known how these conditions interact, clinicians’ ability to identify those a greatest risk and offer effective treatment will be limited.

In summary, dietary intake and physical activity are critical but as yet uninvestigated factors in the expanding body of research seeking to identify the pathogenesis of AED induced weight gain. Isolating contributory health behaviors and psychosocial correlates of abnormal weight gain in children with epilepsy could facilitate the development of novel clinical interventions to mitigate its occurrence as a side effect of epilepsy treatment, thereby reducing the additional risk for obesity related morbidity and mortality and the possible adverse effect of weight gain on compliance with the medical regimen. The current project will provide essential pilot data to support an application for a randomized clinical intervention trial in what would be a new area of epilepsy research.

Primary Aims and Hypotheses

**Aim 1: To Describe Weight Status in Youth with Epilepsy Who Are Prescribed AEDs.**

**Hypothesis 1.1:** Children who are prescribed at least 1 weight positive AED (e.g., valproate, carbamazepine, gabapentin, vigabatrin) will have higher weight status at baseline relative to those not prescribed a weight positive AED (e.g., phenytoin, lamotrigine, levetiracetam, topirimate, felbamate, zonisamide; no medication).

**Hypothesis 1.2:** Children who are prescribed at least 1 weight positive AED will demonstrate an increase in weight status from baseline to follow-up relative to those not prescribed a weight positive AED.
Aim 2: To Examine the Relationship Between Behavioral Health Factors (E.G., Caloric Intake, Energy Expenditure) and Weight Status in Youth on AEDs.

Hypothesis 2.1: At baseline, children on a weight positive AED will report higher caloric intake than children not taking a weight positive AED.

Hypothesis 2.2: Average caloric intake across baseline and follow-up will mediate the relationship between type of AED medication at baseline and change in weight status from baseline to follow-up.

Hypothesis 2.3: At baseline, children on a weight positive AED will demonstrate lower levels of physical activity than children not on a weight positive AED.

Hypothesis 2.4: Average level of physical activity from baseline to follow-up will mediate the relationship between type of AED medication at baseline and change in weight status from baseline to follow-up.

Aim 3: To Assess the Relationship Between Weight Status and Psychosocial Functioning in Terms of Depressive Symptoms and Quality of Life in Youth with Epilepsy

Hypothesis 3.1: At baseline, those on a weight positive AED will report higher levels of depressive symptoms than those not on a weight positive AED.

Hypothesis 3.2: At follow-up, those on a weight positive AED will report higher levels of depressive symptoms than those not on a weight positive AED.

Hypothesis 3.3: At baseline, higher weight status will be associated with more depressive symptoms across groups.

Hypothesis 3.4: Change in weight status from baseline to follow-up will mediate the relationship between type of AED at baseline and depressive symptoms at follow-up.
Hypothesis 3.5: At baseline, those on a weight positive AED will report lower quality of life than those not on a weight positive AED.

Hypothesis 3.6: At follow-up, those on a weight positive AED will report lower quality of life than those not on a weight positive AED.

Hypothesis 3.7: At baseline, higher weight status will be related to lower quality of life across groups.

Hypothesis 3.8: Change in weight status from baseline to follow-up will mediate the relationship between type of AED at baseline and quality of life at follow-up.

Exploratory Analyses

Aim 4: Examine whether the type of AED (weight positive versus not weight positive) is associated with differences in key nutrition variables (e.g., fat, carbohydrates) that are related to weight gain.
<table>
<thead>
<tr>
<th>Weight Positive AED</th>
<th>Accelerated Growth Trajectory</th>
<th>Hypothesized Mechanisms Underlying Weight Gain</th>
</tr>
</thead>
</table>
| Valproate           | Increase rapidly for 3 months, plateau by 6 months | Increased appetite  
Increased thirst  
Increased consumption of carbohydrates  
Decreased energy expenditure  
Reduced basal energy turnover |
| Carbamazepine       | Unknown                        | Edema  
Increased appetite  
Unknown |
| Vigabatrin          | Unknown                        | Increased appetite  
Unknown |
| Gabapentin          | Unknown                        | Unknown |
CHAPTER 2
METHOD

Participants

Participants were 49 youth and their parent or legal guardian recruited at their regularly scheduled visit in the pediatric neurology clinic at Shands Hospital at the University of Florida. Eligible participants met the following inclusion criteria: (1) be between the ages of 8-17; (2) diagnosed with seizures; (3) fluent in English; and (4) accompanied to the appointment by a parent or legal guardian. Parent inclusion criteria were follows: (1) able to read, write, and speak English; (2) lived in the same household as the participating child at least 50% of the time; and (3) did not have any plans to move out the area for the next 9 months. Exclusion criteria included: (1) any child medical condition that would impact weight status (e.g., Prader-Willi syndrome); (2) use of a wheelchair or assisted walking device (e.g., walker); (3) serious psychopathology or other medical or behavioral condition (i.e., schizophrenia, bipolar disorder) that would interfere with the ability to complete study measures; and (4) being on the ketogenic diet. Some children were not able to complete self-report measures due to a cognitive delay; in these cases, parents still completed parent-report measures.

Procedure

The current protocol was approved by the governing IRB. A member of the research team was present in the pediatric neurology clinic on designated days for recruitment. Potential participants were identified by a review of their medical records, and those meeting initial screening criteria were approached as they waited in private patient rooms during their regularly scheduled visit. Parent and child dyads were asked if they would like to hear more about a study examining health status in children with
epilepsy. Families who expressed interest were given more information about the study and completed the informed consent/assent.

Assessments took place at baseline (i.e., the day of recruitment following completion of consent and assent protocol), and at the child’s regularly scheduled appointment in the neurology clinic between 4-6 months post-baseline. For each assessment, families completed a packet of questionnaires that took approximately 45 minutes. At the end of each assessment visit the child was given an accelerometer and instructed to wear it for 7 consecutive days. Families were given a prepaid mailer to return the accelerometer to the research team. If families were unable to attend their follow-up appointments at the neurology clinic or a team member was unable to meet them at this visit, they were provided the opportunity to complete study measures at the PI’s research lab located in Shands Hospital or to have the study measures mailed to them.

Measures

Questionnaires

Child and parent participants completed the following questionnaires and anthropometric measurements at each assessment (see Appendix for all measures):

**Dietary intake** The Block Kids 2004 is a 77-item questionnaire that assessed the child’s dietary intake over the preceding week. The food list for this questionnaire was developed from the NHANES 1999-2002 dietary recall data. The nutrient database was developed from the USDA Nutrient Database for Dietary Studies, version 1.0. The child completed this measure with the help of their parent.

**Energy expenditure** Children wore a Sensewear (Bodymedia, Inc, Pittsburgh, PA) armband accelerometer for 7 days following each assessment visit. The Sensewear
armbands objectively evaluated total energy expenditure and physical activity energy expenditure, steps taken, and intensity expressed as metabolic equivalents (METS) among the children recruited to participate in this study. Children and their parents were instructed in the proper usage of an accelerometer and were given a prepaid mailer for its return. Participants were blinded to the data generated by the armband, which recorded and stored data until it was downloaded to a designated computer with appropriate licensed software. Participants were asked to wear the accelerometer for 7 days only taking the device off to bathe or swim. In line with the extant literature suggesting that 10 hours of daytime wear is considered adherent to assess daytime levels of physical activity (Ekelund, Laun, Sherer, Esliger, Griew, & Cooper, 2012), participants were included if they had at least 10 hours of data for 2 weekdays and 1 weekend day. The first 2 eligible weekdays and first eligible weekend day were selected. Next, minutes spent in sedentary (0 - 2.9 METs), moderate (3.0 – 5.9 METs), vigorous (6.0 – 8.9 METs), and very vigorous (9 METs and above) activity, and average METs was calculated for the 3 selected days. Minutes in moderate, vigorous, and very vigorous activity were summed to determine minutes in physical activity (Ekelund, Luan, Sherer, Esliger, Griew, & Cooper, 2012). Since some individuals wore the accelerometer over night while others did not, minutes spent in sedentary activity was not comparable. Focusing on minutes spent in physical activity (which is not achieved during sleep) therefore targets waking hours is comparable between participants.

**Child health related quality of life** The PedsQL is a 23-item scale that measures health-related quality of life in healthy children and those with acute and chronic conditions. Participants are asked to rate the extent to which items have been a
problem for them in the past month on a 5-point Likert scale with anchors of 0 = never and 4 = always. The PedsQL is comprised of 4 subscales- physical, emotional, social, and academic functioning- as well as an overall quality of life index. Items are reverse scored so that never = 100 and always = 0 with 25 point intervals between response options. Averages are then computed within each subscale and across the 23 items for the overall score. Higher scores indicate better functioning, with 100 signaling no difficulties in functioning. Overall quality of life was used in the present study. The measure has been reported to have excellent internal consistency, clinical validity, and factor-analytic support for subscales (Varni, Seid, & Kurtin, 2001). Both child and parent proxy forms were administered.

**Child behavior and psychosocial functioning** The Behavioral Assessment System for Children (BASC) is a broadband measure of child behavioral and psychosocial functioning. Parents are asked to rate the frequency of each behavior on a 4-point Likert scale (never, sometimes, often, almost always). The child version (BASC-PRS-C) has 134 items and the adolescent version (BASC-PRS-A) has 150 items. The BASC yields T-scores for internalizing and externalizing domains, additional clinical scales, and activities of daily living, as well as subdomains within these areas. The depression subscale within the internalizing domain was used to assess for depressive symptoms in children. In line with the manual for this measure, a T-score of 65 or greater based on age and gender norms were considered to be clinically elevated. The measure was completed by the participating parent. Validity scales were examined to ensure valid response patterns.
Demographic information This questionnaire obtained family background information such as age, gender, race, marital status, education, and family income. This questionnaire also collected information regarding parent and child medical history.

Anthropometrics

Height and weight Child height and weight was obtained from the child’s medical chart at each assessment. In the event that the follow-up assessment was completed outside of a medical appointment, anthropometric measurements were taken by the child’s pediatrician, school nurse, or by their parent.

Medical Records/Chart Review

Medical information Starting from the date of the epilepsy diagnosis, children are typically seen in the pediatric neurology clinic every 4-6 months. Information on height and weight, the type of seizure disorder (i.e., generalized, partial, or unclassified), time since diagnosis, anti-epileptic medication and other medication usage, dosage of medication, medical comorbidities, and psychiatric comorbidities was collected from the child's medical chart at baseline and the follow-up assessment.

Statistical Analyses

All statistical analyses were conducted using the Statistical Package for the Social Sciences, (SPSS, version 17.0, SPSS Inc., Chicago, Illinois).

Sample Size

This was the first project investigating the impact of health behaviors on weight status change in children on AED medication, and thus there was no existing data to guide power analyses. A sample size of 50 child/parent dyads gave .94 power to detect an effect size of .5 at follow-up.
Preliminary Data Analyses

Height and weight were converted first into BMI using the Quetelet formula \( \text{BMI} = \frac{\text{weight (kg)}}{\text{height (cm}^2\text{)} \text{]} \), and then into BMI z-scores, which plots child weight status relative to other children who are the same age and gender. BMI z-score change was then calculated by subtracting their weight status at baseline from their weight status at follow-up. A positive BMI z-score change indicates increased weight status from baseline to follow-up while a negative change score indicates reduced weight status over the study period. For descriptive purposes, children were also classified into underweight, healthy weight, overweight, and obese weight status categories based on widely accepted cutoffs (e.g., Cole, Bellizzi, Flegal & Dietz, 2000).

Children were separated into three groups: (1) children prescribed at least 1 weight positive AED; (2) children not prescribed a weight positive AED (i.e., children taking weight neutral or negative AEDs or those not taking any AED); (3) children who were placed on, or taken off a weight positive AED during the course of the study. Those children in category 3 were excluded from analyses because the relationship between category of AED and change in weight status, behavioral health factors, and psychosocial functioning could not be assessed consistently over time.

Upon examination of the medication status of child participants, it was discovered that only 11 children used weight positive AED, while 34 used non-weight positive AED. To adjust for the significant imbalance between groups frequency matching was used to select a subset of participants from the non-weight positive group who were similar to the weight-positive group in age, gender, and race/ethnicity. The decision to match on these characteristics was guided by literature indicating that caloric intake and physical activity vary across these parameters (USDA, 2010). For instance, average level of
physical activity declines during adolescence, especially among females (Troiano, Berrigan, Dodd, Masse, Tilert, & MacDowell, 2008; Zametkin, Zoon, Klein, & Munson, 2004). In addition, one of the critical developmental periods for childhood-onset obesity occurs during early adolescence, especially for females (Dietz, 1994). Children from minority backgrounds are more likely to have a higher weight status than their non-minority peers (Ogden, Carroll, Kit, & Flegal, 2012; Zametkin et al., 2004). Most importantly, matching participants on demographic characteristics provided a way to control for these confounds a priori since the small sample size precluded the inclusion of these variables as covariates (Ahmed, Fatmi, Siddiqui, & Sheikh, 2011; Christoffel, Donovan, Shofer, Wills, & Levine, 1996).

Preliminary data analyses included independent t-tests to determine whether participants that completed both baseline and time 2 assessment (completers) differed from those that did not complete time 2 assessment (non-completers) on age, weight status, caloric intake, or minutes spent in physical activity. Following the matching procedure whereby a subset of individuals from the non-weight positive group were selected to match cases in the weight positive group on gender, age, and race/ethnicity, independent t-tests were again used to assess for differences between those cases selected for analysis and those not selected for analysis across independent and dependent variables.

**Primary Analyses**

Independent samples t-tests were used to assess for baseline differences between the weight positive and non-weight positive group in weight status, total caloric intake, minutes spent in any physical activity (i.e., > 3 METs), quality of life, and depressive symptoms. Analysis of variance (ANOVA) was used to test for group
differences in change in weight status over time. Pearson product moment correlations were calculated between baseline BMI z-score, and depressive symptoms and quality of life at baseline and follow-up to determine the direction and strength of the relationships. Then, multiple regression analysis was used to test for mediation. The steps to test mediation outlined by Baron and Kenny (1986) are as follows: establish a significant relationship between the predictor (AED at baseline) and the outcome (weight status at follow-up); (2) establish a relationship between the predictor and the mediator (average caloric intake across baseline and follow-up); (3) show that after controlling for the relationship between the predictor and the mediator, the mediator predicts the outcome; and (4) show that the reduction in the strength of association between the predictor and the outcome is significant in the presence of the mediator using a Sobel test.

Psychosocial measures were examined for missing data. On the PedsQL, if >80% of data points were present on individual subscales, mean substitution based on subscale scores was used to impute missing data points.

**Exploratory Analyses**

Independent samples t-tests were used to test for group differences in fat intake and carbohydrate intake at baseline.
CHAPTER 3
RESULTS

Preliminary Analyses

Demographic information is presented by group in Table 3-1. Overall, 49 families were recruited into the study. Participants were 7-17 years old (M=12.3; SD=2.8). The majority of child participants was Caucasian (67.3%), followed by African American (16.3%), Hispanic (4.1%), Bi-racial (4.1%), Asian (2.0%), and Other/Not reported (6.1%). The vast majority of participating adults were mothers (79.6%), though fathers (14.3%), grandparents (2.0%), and step-parents (2.0%) were also included. The majority of caregivers were currently married (69.4%). Median income was $40,000-$49,999. Across the whole sample, 38 families (78%) completed the follow-up assessment. Independent t-tests were used to test for differences between completers and non-completers. Results indicated that the groups did not differ in terms of age, caloric intake, minutes spent in physical activity, quality of life, depressive symptoms, or BMI z-score at baseline.

Of the total sample, 11 children were on weight-positive medication and 34 were in the non-weight positive category (i.e., they were taking weight neutral or weight negative medication, or not taking any medication) (Figure 3-1). Four individuals were put or taken off of a weight positive AED during the course of the study and were therefore excluded from analyses. Of the 34 youth in the non-weight positive group, 5 did not complete the dietary intake questionnaire at baseline and 1 did not complete the questionnaire at follow-up and were also excluded from further analysis, reducing that group size to 28. Reasons for incomplete data collection included having to leave early, failing to return the measures via mail, and administrative error. Three of the remaining
individuals in the weight positive group and 2 in the non-weight positive group did not complete follow-up, reducing the eligible number of participants in each group to 8 and 26, respectively.

Of the 8 children in the weight positive group who completed follow-up, 1 was non-adherent to the accelerometer at baseline while 2 more were non-adherent to the accelerometer at follow-up. This meant that only 5 families in the weight-positive group had complete physical activity data across follow-ups. To protect the small sample size from further loss, it was decided that families who completed the entire baseline assessment, including having physical activity data, and who completed the follow-up assessment with or without physical activity data would be maintained. As a result, analysis of physical activity data would be limited to baseline. On the basis of these revised inclusion criteria, there were 7 eligible families in the weight-positive group. Six children did not have accelerometer data at baseline in the non-weight positive group, leading to a sample size of 20.

To allow for the control of covariates and balance group size, it was decided that frequency matching would be used to select a subset of participants in the non-weight positive group for analysis. After obtaining several statistical consultations, this approach was judged to be the most scientifically sound given the small sample size and unbalanced groups. Seven cases from the non-weight positive group, out of 20 eligible, were selected to match the frequency of age, gender, and minority status variables in the weight-positive group (Table 3-2). Only 4 individuals out of the eligible 20 in the non-weight positive group were of minority status, thus those 4 were selected for inclusion to match the frequency (i.e., 4) of minorities in the weight positive group.
Three out of those 4 selected participants were male, which also fulfilled the frequency of males needed to match the weight-positive group. Lastly, 3 more individuals were selected from the eligible non-weight positive sample to match the distribution of ages in the weight-positive group. To ensure systematic selection, the first 3 individuals based on date of recruitment who were of the needed ages were selected for inclusion.

Independent t-tests were used to assess whether the selected group of matched cases from the non-weight positive group differed from the larger group from which they were drawn on any of the variables of interest. Results suggested no significant differences in caloric intake, minutes spent in physical activity, quality of life, depressive symptoms, or BMI z-score at baseline. Nor were there significant differences in change in BMI z-score from baseline to follow-up.

Demographic characteristics, health status, epilepsy type, time since diagnosis, and number of AED medications for the final sample are presented in Table 3-3. In the weight positive group, 4 youth had generalized, 1 had partial, and 2 had unclassified seizures. In the other group, all 7 had generalized seizures. Etiology of seizures in the weight positive group was more varied with 5 having idiopathic epilepsy and 2 having symptomatic epilepsy. In the non-weight positive group, all 7 had idiopathic epilepsy. While not tested statistically, visual inspection of the data suggests that youth in the weight positive group were less likely to have well-controlled epilepsy. Within that group, 3 participants had daily or weekly seizures, 2 had seizures monthly, 1 had seizures yearly, and only 1 had seizures less than yearly. By comparison, in the non-weight positive group, 2 individuals had daily or weekly seizures, 1 had seizures monthly, 1 had seizures yearly, and 3 participants had seizures less than yearly. The majority of
participants in both conditions were on monotherapy (6 weight positive; 4 non-weight positive), and there was 1 individual in each group on polytherapy. The remaining 2 participants in the non-weight positive group were not taking AED medication. The majority of participants in each group had been diagnosed greater than 2 years earlier (71% in each group). Only one participant (14%) in each group had been diagnosed with epilepsy within 6 months of baseline. Finally, based on parent report and review of medical records, 6 participants (86%) of individuals in the weight positive group had been diagnosed with a developmental disorder (e.g., autism, developmental delay) while only 2 individuals (29%) in the non-weight positive group had a developmental problem. Two individuals in the non-weight positive group were diagnosed with ADHD and Oppositional Defiant Disorder, respectively. No additional psychiatric diagnoses were documented for the weight-positive group. In terms of additional health conditions, 5 individuals in the weight-positive group had comorbid medical diagnoses that included gingival hyperplasia, genetic disorder, NOS, antiphospholipid syndrome, cerebral palsy, static encephalopathy, subdural hematoma, and encephalitis. Only one person in the non-weight positive group had additional medical diagnoses (i.e., borderline diabetes, obesity, and obstructive sleep apnea).

**Aim 1 - Weight Status Between Groups**

Independent samples T-test was used to assess for differences in baseline weight status between groups [t(12) = -1.41, p = .18]. Those in the weight positive group (Mean BMI z-score = -.28, SD = 1.86, range -3.18 – 1.73) did not have a significantly higher weight status as baseline than those in the non-weight positive group (Mean BMI z-score = .98, SD = .54, range -1.10 - 2.90) (Table 3-3). For descriptive purposes participants were categorized into widely accepted weight status categories based on
BMI percentile. In the weight positive group, 2 children were classified as underweight, 3 as healthy weight, 1 as overweight, and 1 as obese. In the non-weight positive group, 3 youth were classified as healthy weight and 4 as obese. While not tested statistically, there appeared to be more variability in categorical weight status in the weight positive group, and a greater tendency towards being obese in the non-weight positive group.

Analysis of variance was used to examine the change in weight status (i.e., change in BMI z-score) from baseline to follow-up between those on weight positive AEDs and those not on weight positive AEDs. No differences in change in weight status from baseline to follow-up emerged between the weight positive group (M = -.52; SD = 1.26) and the other group (M = -.07, SD = .31) [F(1,12) = .86, p = .377].

Aim 2 - Behavioral Health Factors Between Groups

Information about behavioral health factors by group is presented in Table 3-4. Independent samples t-test was used to assess for differences in caloric intake at baseline between groups. Those on weight positive AEDs (M = 1797.88, SD = 586.54) did not report significantly greater caloric intake than those not on weight positive AEDs (M = 1740.95, SD = 1080.64) [t(12) = .12, p = .90].

Multiple regression analysis was used to examine whether average caloric intake mediated the relationship between type of AED at baseline and change in weight status. In line with procedures outlined by Baron and Kenny (1986), the path between the exogenous (group membership) and endogenous (weight status) variable was tested first. Type of AED at baseline did not significantly predict change in weight status (R² = .26, F[1,12] = .86, p = .37) (Figure 3-2). Therefore, mediation was not possible.

Next, independent samples t-tests were used to examine baseline differences in minutes in physical activity between groups. Those in the weight positive group (M =
365.42, SD = 313.27) did not exhibit significantly lower levels of physical activity than those in the non-weight positive group (M = 424.29, SD = 207.90) (t[12] = -.41, p = .69). As stated above, group membership did not predict change in weight status from baseline to follow-up (R² = .26, F[1,12] = .86, p = .37); therefore, minutes spent in physical activity could not assessed as a mediator of this relationship (Figure 3-3).

**Aim 3 - Psychosocial Functioning Between Groups**

Upon examination of the PedsQL data, it was discovered that 1 participant failed to answer 1 item (out of 8) on the physical subscale of the parent proxy report at follow-up. Therefore, the mean response was calculated using the rest of the items on that subscale and substituted for the missing value.

Pearson product moment correlations were calculated to determine the strength and direction of relationships between weight status and psychosocial variables at baseline (Table 3-5). At baseline, moderate but non-significant positive correlations were found between weight status and depressive symptoms (r = .48) and weight status and quality of life (r = .40). This means that higher weight status was related to both higher levels of depressive symptoms and better quality of life. Correlations between baseline weight status and follow-up levels of depressive symptoms (r = .17) and quality of life (r = -.05) were weak. Significant correlations were observed between depressive symptoms at baseline and follow-up (r = .59, p < .05). While not significant, moderate stability was also found between serial measurements of quality of life (r = .45). Finally, depressive symptoms at baseline strongly predicted quality of life at follow-up (r = -.74, p < .01) meaning that higher levels of depressive symptoms at baseline were related to lower quality of life at follow-up.
Levels of psychosocial variables by group are presented in Table 3-6. Independent samples t-tests revealed that the weight positive group (M = 59.94, SD = 11.29) reported significantly worse quality of life than the non-weight positive group (M = 80.43, SD = 11.24) at baseline (t[12] = -3.40, p < .01). At follow-up, the groups did not differ in quality of life (t[12] = -1.66, p = .12). No group differences emerged in level of depressive symptoms at baseline (t[12] = .43, p = .67) or follow-up (t[12] = -.72, p = .49). The average level of depressive symptoms across groups and assessment points was in the non-depressed range. Two individuals (28.6%) in the weight-positive group and 1 individual (14.3%) in the non-weight positive group reported levels of depressive symptoms above the clinical cutoff of T = 65 at both baseline and follow-up.

Finally, linear regression was used to determine whether group membership predicted depressive symptoms and quality of life at follow-up. Results suggested that group status was not significantly predictive of depressive symptoms (R² = .04, F[1,12] = .52, p = .49) (Figure 3-4) or quality of life (R² = .19, F[1,12] = .2.74, p = .12) (Figure 3-5) at follow-up. As a result of these non-significant paths, further investigation as change in weight status as a mediator for these relationships was not conducted.

**Exploratory Analyses**

Independent samples T-tests were used to determine whether groups significantly differed in terms of key nutrients at baseline. Those in the weight positive group did not exhibit significantly different intake of calories from fat (M=69.86, SD = 20.72) than those in the non-weight positive group (M = 71.78, SD = 48.89) [t(12) = -.10, p = .93]. Similarly, no group differences emerged in calories from carbohydrates (weight positive M = 222.04, SD = 81.30; non-weight positive M = 220.66, SD = 138.97) [t(12) = .02, p = .98].
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weight Positive</th>
<th>Non Weight Positive</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>11</td>
<td>34</td>
<td>4</td>
</tr>
<tr>
<td>Child Age</td>
<td>14.0 (2.5)</td>
<td>11.9 (2.8)</td>
<td>11.5 (2.1)</td>
</tr>
<tr>
<td>Boys/Girls (n)</td>
<td>6/5</td>
<td>13/21</td>
<td>3/1</td>
</tr>
<tr>
<td>Adult Participant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>9</td>
<td>27</td>
<td>3</td>
</tr>
<tr>
<td>Father</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Two parent households (%)</td>
<td>55</td>
<td>74</td>
<td>75</td>
</tr>
<tr>
<td>Child Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>5</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>African American</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Bi-racial</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Not reported</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Family Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below $19,999</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>$20,000-$59,999</td>
<td>5</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Over $60,000</td>
<td>3</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Not reported</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Completed follow-up (n)</td>
<td>8</td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>BMI z-score baseline</td>
<td>-0.1 (1.8)</td>
<td>1.0 (1.1)</td>
<td>1.1 (1.5)</td>
</tr>
<tr>
<td>BMI z-score follow-up</td>
<td>-0.4 (2.6)</td>
<td>0.9 (1.2)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Table 3-2. Gender, Minority Status, and Age for All Participants Entered into the Frequency Match Procedure

<table>
<thead>
<tr>
<th>Participant</th>
<th>Group</th>
<th>Selection Status</th>
<th>Gender</th>
<th>Age</th>
<th>Minority Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>16</td>
<td>Minority</td>
</tr>
<tr>
<td>2</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>16</td>
<td>Minority</td>
</tr>
<tr>
<td>3</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>11</td>
<td>Minority</td>
</tr>
<tr>
<td>4</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>15</td>
<td>Caucasian</td>
</tr>
<tr>
<td>5</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>8</td>
<td>Minority</td>
</tr>
<tr>
<td>6</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>14</td>
<td>Caucasian</td>
</tr>
<tr>
<td>7</td>
<td>Weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>13</td>
<td>Caucasian</td>
</tr>
<tr>
<td>8</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>11</td>
<td>Minority</td>
</tr>
<tr>
<td>9</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>17</td>
<td>Caucasian</td>
</tr>
<tr>
<td>10</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>12</td>
<td>Minority</td>
</tr>
<tr>
<td>11</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>15</td>
<td>Caucasian</td>
</tr>
<tr>
<td>12</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>16</td>
<td>Caucasian</td>
</tr>
<tr>
<td>13</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>F</td>
<td>11</td>
<td>Minority</td>
</tr>
<tr>
<td>14</td>
<td>Non weight-positive</td>
<td>Selected</td>
<td>M</td>
<td>9</td>
<td>Minority</td>
</tr>
<tr>
<td>15</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>11</td>
<td>Caucasian</td>
</tr>
<tr>
<td>16</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>12</td>
<td>Caucasian</td>
</tr>
<tr>
<td>17</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>8</td>
<td>Caucasian</td>
</tr>
<tr>
<td>18</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>10</td>
<td>Caucasian</td>
</tr>
<tr>
<td>19</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>8</td>
<td>Caucasian</td>
</tr>
<tr>
<td>20</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>M</td>
<td>13</td>
<td>Caucasian</td>
</tr>
<tr>
<td>21</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>11</td>
<td>Caucasian</td>
</tr>
<tr>
<td>22</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>12</td>
<td>Caucasian</td>
</tr>
<tr>
<td>23</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>M</td>
<td>17</td>
<td>Caucasian</td>
</tr>
<tr>
<td>24</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>12</td>
<td>Caucasian</td>
</tr>
<tr>
<td>25</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>10</td>
<td>Caucasian</td>
</tr>
<tr>
<td>26</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>11</td>
<td>Caucasian</td>
</tr>
<tr>
<td>27</td>
<td>Non weight-positive</td>
<td>Not selected</td>
<td>F</td>
<td>11</td>
<td>Caucasian</td>
</tr>
</tbody>
</table>
Table 3-3. Demographics, Epilepsy Type, Time Since Diagnosis, Seizure Frequency, Medications, and BMI Z-Scores by AED Group for Matched Sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weight Positive</th>
<th>Non Weight Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Child Age</td>
<td>13.3 (2.9)</td>
<td>13.0 (3.0)</td>
</tr>
<tr>
<td>Boys/Girls (n)</td>
<td>3/4</td>
<td>3/4</td>
</tr>
<tr>
<td>Child Race/Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>African American</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Bi-racial</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Family Income</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below $19,999</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>$20,000-$59,999</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Over $60,000</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Not reported</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Type of Epilepsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Partial</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Time Since Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 6 months</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Within 2 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Greater than 2 years</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Seizure Frequency at Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily/Weekly</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Monthly</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Yearly</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Less than Yearly</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Number of AED Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>One</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Two</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Co-morbid Developmental Disorder</td>
<td>6 (86%)</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>Co-morbid Medical Diagnosis</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>BMI z-score baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Healthy (n)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Overweight (n)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Obese (n)</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 3-3. Continued

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weight Positive</th>
<th>Non Weight Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI z-score follow-up</td>
<td>-0.8 (2.6)</td>
<td>0.9 (1.5)</td>
</tr>
<tr>
<td>BMI z-score range, follow-up</td>
<td>-4.12 – 1.87</td>
<td>-1.48 – 2.31</td>
</tr>
<tr>
<td>BMI z-score change</td>
<td>-0.52 (1.26)</td>
<td>-0.07 (.31)</td>
</tr>
</tbody>
</table>
Table 3-4. Behavioral Health Factors by AED Group for Matched Sample

<table>
<thead>
<tr>
<th>Health Behavior</th>
<th>Weight Positive (N=7)</th>
<th>Non Weight Positive (N=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dietary Intake</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total caloric intake, baseline</td>
<td>1797.88 (586.54)</td>
<td>1740.95 (1080.64)</td>
</tr>
<tr>
<td>Total caloric intake, follow-up</td>
<td>1397.68 (556.18)</td>
<td>1494.79 (62.72)</td>
</tr>
<tr>
<td>Calories from fat, baseline</td>
<td>69.86 (20.72)</td>
<td>71.78 (48.89)</td>
</tr>
<tr>
<td>Calories from carbohydrates, baseline</td>
<td>222.04 (81.30)</td>
<td>220.66 (138.97)</td>
</tr>
<tr>
<td><strong>Physical Activity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minutes in sedentary activity, baseline</td>
<td>3443.29 (348.40)</td>
<td>3690.57 (225.55)</td>
</tr>
<tr>
<td>Minutes in moderate activity, baseline</td>
<td>320.71 (264.79)</td>
<td>386.86 (186.48)</td>
</tr>
<tr>
<td>Minutes in vigorous activity, baseline</td>
<td>43.43 (53.48)</td>
<td>36.00 (40.51)</td>
</tr>
<tr>
<td>Minutes in very vigorous activity, baseline</td>
<td>1.29 (2.36)</td>
<td>1.43 (1.90)</td>
</tr>
<tr>
<td>Average METs, baseline</td>
<td>1.58 (0.31)</td>
<td>1.64 (0.20)</td>
</tr>
<tr>
<td>Variable</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>1. BMI z-score baseline</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>2. BASC depression, baseline</td>
<td>.48</td>
<td>--</td>
</tr>
<tr>
<td>3. BASC depression, follow-up</td>
<td>.17</td>
<td>.59*</td>
</tr>
<tr>
<td>4. QOL, baseline</td>
<td>.40</td>
<td>-.20</td>
</tr>
<tr>
<td>5. QOL, follow-up</td>
<td>-.05</td>
<td>-.74**</td>
</tr>
</tbody>
</table>

* p<.05; ** p<.01
Table 3-6. Psychosocial Functioning by Group for Matched Sample

<table>
<thead>
<tr>
<th>Psychosocial factor</th>
<th>Weight Positive</th>
<th>Non Weight Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=7)</td>
<td>(N=7)</td>
</tr>
<tr>
<td><strong>BASC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms, baseline (t-score)</td>
<td>54.43 (12.90)</td>
<td>51.29 (14.19)</td>
</tr>
<tr>
<td>N at or above clinical cutoff, baseline</td>
<td>2 (28.6%)</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Depressive symptoms, follow-up (t-score)</td>
<td>47.43 (25.10)</td>
<td>54.71 (9.27)</td>
</tr>
<tr>
<td>N at or above clinical cutoff, follow-up</td>
<td>2 (28.6%)</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td><strong>PedsQL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of life, baseline</td>
<td>59.94 (11.29)</td>
<td>80.43 (11.24)</td>
</tr>
<tr>
<td>Quality of life, follow-up</td>
<td>63.20 (16.79)</td>
<td>78.42 (17.58)</td>
</tr>
</tbody>
</table>
Participants Recruited: N=49

Participants Excluded: N=4 starting or stopping a weight positive drug during course of the study.

Weight Positive: N=11

Participants lost to follow-up: N=3

Weight Positive: N=8

Participants Excluded: N=1 No baseline accelerometer data

Non-Weight Positive: N=34

Participants Excluded: N=6 did not complete dietary intake

Non-weight Positive: N=26

Participants lost to follow-up: N=2

Participants Excluded: N=6 No baseline accelerometer data

Non-weight Positive: N=20

Non-weight Positive Participants Matched for Analysis: N=7

Non-weight Positive Participants Not Selected for Analysis: N=13

Figure 3-1. Participant Flow Chart
Figure 3-2. Proposed Mediation of AEDs and Change in Weight Status by Average Caloric Intake
Figure 3-3. Proposed Mediation of AED and Change in Weight Status by Physical Activity
Figure 3-4. Proposed Mediation Model for AED and Depressive Symptoms by Change in Weight Status
Figure 3-5. Proposed Mediation Model for AED and Quality of Life by Change in Weight Status

\[ B = 0.43, \ p = 0.12 \]
CHAPTER 4
DISCUSSION

Anti-epileptic medications are the first line of treatment in pediatric epilepsy. Up to 65% of children on AEDs eventually become seizure free, often within the first 2 years of medical therapy. A few of these medications have been associated with accelerated weight gain (see Biton, 2003b for review), which could increase the risk for obesity related medical and psychosocial comorbidities. Significant weight gain as a side effect of treatment could contribute to the high rates of non-adherence in this population (Modi, Ingerski, Rausch, & Glauser, 2011), especially among body-conscious adolescents (Daniels, Nick, Liu, Cassedy, & Glauser, 2009). The etiology of increased growth velocity remains unknown but has been theorized to include increased appetite, decreased energy expenditure, and reduced basal energy turnover (Biton, 2003b). To our knowledge, this is the first study that assessed the relationship between AEDs and critical, modifiable health behaviors that regulate caloric balance and therefore weight status (USDA, 2010). Both youth with epilepsy and those of overweight and obese weight status are at greater risk for psychosocial impairment than their healthy, normal weight peers (e.g., Eremis et al., 2004; Leonard & George, 1999; Pellock, 2004; Zeller & Modi, 2008). We also assessed depressive symptomatology and quality of life to determine whether AED induced weight gain leads to additional psychosocial difficulties in youth with epilepsy.

Aim 1- AEDs and Weight Status

It was hypothesized that children taking a weight positive AED would demonstrate higher weight status at baseline and greater increases in weight status over time compared to children on weight neutral or negative AEDs or those not taking AEDs.
Neither of these predictions was supported by the present data. Although there were no significant differences in mean BMI z-score between groups at baseline, there appeared to be a greater tendency towards overweight or obesity in the non-weight positive group when looking at weight status from a categorical perspective. Specifically, at baseline 2 individuals (29%) were overweight or obese in the weight positive group compared to 4 participants (57%) in the non-weight positive group, contrary to expectations. No significant differences emerged between groups over time.

Given that the majority of participants had been diagnosed with epilepsy greater than 2 years ago, our inability to detect group differences in growth velocity over time is not surprising. Existing research on the weight-related impact of valproate (Depakote) has generally suggested that the period of increased growth velocity occurs within the first 3 months of treatment, stabilizes by 6 months, and then plateaus for the duration of treatment (Biton, 2003b; Demir & Aysun, 2000; Egger & Brett, 1981; Novak et al., 1999). However, one study found that in younger children the period of increased growth velocity can span 16 months (Grosso et al., 2009). The trajectory of accelerated weight gain has not been established for the other AEDs most consistently associated with weight gain (i.e., carbamazepine, gabapentin, and vigabatrin). If children had been taking weight positive medication for longer than 6 months, it is very likely that this important window of accelerated growth velocity was not captured by the present study. Therefore, children in weight positive group would not be gaining weight more rapidly than those in the other group as a result of medication side effects.

Under the assumption that the accelerated weight gain had already taken place, it was anticipated that children on weight positive AEDs at baseline would still exhibit a
higher weight status compared to those on weight neutral, negative, or no AEDs, since extant literature suggests that increased weight status is maintained over the duration of treatment (Biton, 2003b). Yet, those on weight-positive AEDs at baseline did not demonstrate higher weight status than those in the non-weight positive group. There are several potential explanations for these findings. First, even when focusing on valproate, the AED most strongly associated with weight gain, only 45-60% of youth experience this side effect (Egger & Brett, 1981; Wirrell, 2003). The prevalence of accelerated weight gain amongst the other weight positive AEDs ranges from 5-25% (Biton, 2003b; Easter et al., 1997). Therefore, the base rate for affected children in our study could potentially be quite low given the sample size and render it difficult to assess. Second, children with epilepsy are more likely to present at diagnosis with higher rates of both underweight and overweight compared to healthy controls (Daniels et al., 2009) and to have a higher weight status over time than healthy age-matched peers (Wong & Wirrell, 2006). While we did not capture weight status at diagnosis, by baseline, 43% of youth in our study had BMIs in the overweight or obese range which exceeds the national rate of 33% in children aged 6-19 years (Ogden et al., 2012). Indeed, less than half of the children in our study fell in the healthy weight status range. Armed with this information, clinicians may be inclined to consider potential weight effects when deciding between equally effective medications to promote weight gain among individuals with preexisting underweight and weight loss in those in the overweight or obese range, which over time may theoretically produce less variability in weight status between children on different medications over time.
Etiology has been related to weight status among children with epilepsy (Daniels et al., 2009). Children with symptomatic seizures are at greater risk to have a weight status under the 10th percentile while those with idiopathic seizures are at greater risk for being overweight. Additionally, children with intractable epilepsy are more likely than healthy peers to experience growth failure, especially those with comorbid neurological conditions (Bergqvist, Trabulsi, Schall, & Stallings, 2008). While not tested statistically, there were more individuals with symptomatic and uncontrolled epilepsy in the weight positive group, as well as more individuals with comorbid developmental problems. It is possible that one or more of these factors was suppressing growth velocity accelerations or that AED induced weight gain had helped to normalize their weight status relative to peers. By excluding individuals on the ketogenic diet and those who were non-ambulatory, we likely eliminated many others who would be on the lower end of the weight spectrum. A larger trial would be necessary to investigate potential interactions between seizure type, etiology, comorbid neurological problems, and AED-induced weight gain.

**Behavioral Health Factors**

**Dietary Intake**

Increased appetite has been proposed as one of the mechanisms underlying accelerations in growth velocity for weight-positive AEDs. The behavioral proxy of appetite is dietary intake which should theoretically increase when appetite is stimulated. If increased appetite is indeed a factor contributing to changes in weight velocity, it was hypothesized that this could be captured via level of caloric intake such that those on weight positive AEDs would report higher caloric intake at baseline compared to those not on weight-positive medications. We also predicted that average
caloric intake from baseline to follow-up would mediate the relationship between type of AED at baseline and weight status change over time, meaning that higher levels of caloric intake explain why appetite stimulating medications are associated with increasing weight status.

Contrary to expectations, those taking weight positive AEDs did not report higher caloric intake at baseline compared to those on weight neutral, negative, or no AEDs. In addition, type of AED at baseline was not related to weight status change over time precluding examination of caloric intake as a mediator of growth velocity. The average level of daily caloric intake at baseline in the weight positive group (M = 1798, S.D. = 587) and non-weight positive group (M = 1741; S.D. = 1080) was slightly lower than the nationally reported intake in children and adolescents (1897 - 2218 kcal/day) in the NHANES III survey (McDowell, Briefel, Alaimo, Bischof, et al., 1994). Only 4% of calories per day were reported to come from fat and only 12% of calories from carbohydrates. These figures are well below the nationally reported intake of fat (~35%), as well as in conflict with data finding that carbohydrates constitute the greatest source of calories in the American diet (USDA, 2010). At follow-up, average daily caloric intake fell to between 1400 and 1500 calories per day across groups. Comparing these results to those from NHANES III database suggests that current estimates of intake may be low.

The lack of significant group differences in caloric intake is not surprising given that the groups did not differ in weight status at baseline or over time. Again, given the small sample size used for data analysis, potentially low prevalence of weight gain as a side effect, and time since diagnosis, it is possible that dietary intake is a contributory
factor in accelerated growth velocity but was not adequately captured in the current study. Differences in intake over time may reflect the assessment environment. At baseline, the child and participating adult completed the dietary intake measure together under the supervision of a research assistant. At follow-up, many of the families completed the assessments remotely. It is possible that the nutritional surveys were completed independently by the child rather than in collaboration with the parents at follow-up, and consequently that the reported variety and/or portion sizes of foods consumed were less accurate. Future studies seeking to elucidate the pathogenesis of AED induced weight gain should measure dietary intake pre- and post-AED initiation and consider using the gold standard of nutritional assessment, 3-day dietary recalls completed with the child and parent, if time and resources allow.

Individuals on the ketogenic diet (excluded from the present study) have been the virtual sole focus of studies assessing dietary intake in youth with epilepsy. The high fat, low carbohydrate regimen can sometimes reduce seizures in those with medically refractory disease (Neal, Chaffe, Schwartz, Lawson, Edwards et al., 2008). Research has shown that intractable epilepsy is associated with lower caloric intake, poorer nutritional status, and growth retardation (Volpe, Schall, Gallagher, Stallings, & Bergqvist, 2007). The ketogenic diet in itself produces declining weight status (Liu, Williams, Basualdo-Hammond, Stephens, & Curtis, 2003). In contrast to the expanding body of research focusing on children at the bottom of the growth curve, little attention has been paid to assessing nutritional intake and growth among youth with epilepsy at the other end of the weight spectrum. Considering the high rates of overweight and obesity among youth (Ogden et al., 2012), the increased tendency towards overweight
among children with epilepsy (Daniels et al., 2009; Modi, Ingerski, Rausch, & Glauser, 2011), and the association of certain AEDs with increased weight gain (Biton, 2003a,b), endocrine (Aydin, Serdologlu, Okuyaz, Bideci, Gucuyener, 2005; Verotti et al., 2002), and biochemical changes (Isojarvi et al., 1998), this population may be particularly vulnerable to unhealthy weight status and consequently to obesity related medical and psychosocial comorbidities. Interventions targeting dietary intake may be more effective in reducing weight status among youth compared to attempts to increase physical activity (Spear et al., 2007). Understanding nutritional intake in this population is the necessary first step to developing interventions to promote healthy weight status.

**Physical Activity**

Physical activity also regulates weight status through its impact on energy balance, and thus we hypothesized that lower levels of physical activity among youth on weight positive AEDs secondary to fatigue or lethargy could also explain increased growth velocity. This was not supported by the present data. Youth on weight positive AEDs did not spend significantly more minutes in physical activity over the course of 3 days (M = 367) than those on non-weight positive AEDs (M = 426). Since the groups did not differ in weight status change over time, physical activity was not explored as a mediator. One important finding was that, across groups, youth on average spent more than 2 hours per day in physical activity (>3 METs), more than doubling the national guidelines for physical activity of 60 minutes per day in this age group (USDA, 2010). These results are somewhat inconsistent with literature on activity patterns in children with epilepsy suggesting this population may engage in less physical activity than healthy peers or siblings (Van Empelen et al., 2005; Wong & Wirrell, 2006). However, these previous studies used parent and self-reports of physical activity instead of
objective measures of energy expenditure such as accelerometry, which was used in the current study. Additionally, children with epilepsy have been found to engage in fewer group-based physical activities which confer benefits not only through physical conditioning but also increased opportunity for peer socialization (Wong & Wirrel, 2006). The latter is important as youth with epilepsy report feeling socially withdrawn (McEwan, Espie, Metcalfe, Brodie, & Wilson, 2004). We did not document the types of physical activities that youth were engaged in, whether individual versus group-based, or recreational versus organized sports. It will be important for future studies to not only measure energy expenditure objectively but also record how children spend their time.

Research on physical activity and physical fitness in children has shown that overall levels of daily physical activity are significantly correlated to cardiorespiratory fitness measured by $V_{O2peak}$, and that this relationship is stronger for intensity in the vigorous range (Dencker, Thorsson, Karlsson, Linden, Svenssen, et al., 2006). A recent meta-analysis of studies published from the International Children’s Accelerometry Database representing more than 20,000 children found that more time the child spent in daily moderate to vigorous activity, the better the person’s cardiometabolic profile (Ekelund, Luan, Sherar, Esliger, Griew, & Cooper, 2012), which reduces risk for obesity related comorbidities such as type 2 diabetes and coronary disease. Existing literature suggesting that children with epilepsy are less active than healthy peers is concerning in part because they may not be achieving healthy fitness levels. Indeed, studies of physical fitness in adults with epilepsy have indicated lower levels of endurance, strength, flexibility, and cardiorespiratory fitness compared to the general population (Nakkan et al., 1990; Steinhoff et al., 2005). Similar data is not
available for children with epilepsy. Results from the present study are encouraging in that they show that at least among those in our sample, children on average are spending enough time in sufficiently intense activities to potentially reap these benefits. However, we did not measure fitness or assess biochemical markers such as cholesterol or insulin resistance. Future studies examining physical activity in this population should include objective measures of cardiorespiratory and metabolic functioning.

Our physical activity findings must be interpreted with caution. First, it is possible that that youth who were compliant with the accelerometer may have been more active than their non-adherent counterparts. Additionally, there is a tendency for studied behaviors to increase (Campbell, Maxey, & Watson, 1995; Vehmas, 1997), so that youth may have been inclined to be more active than usual on days that they were wearing the accelerometer. Due to a lack of power, we could not look at predictors of physical activity, such as seizure control. Lastly, our small sample size makes it difficult to generalize any findings.

**Psychosocial Functioning**

Across all individuals in our study, higher levels of depressive symptoms at baseline were significantly correlated to higher levels of depressive symptoms and worse quality of life at follow-up. Concurrent ratings of depressive symptoms and quality of life at baseline and follow-up were not related. As depressive symptoms intensify over time, changes in mood, activity level, concentration, energy, sleep, and appetite may translate into impairments in HRQOL. Chronic comorbid internalizing disorders have been strongly tied to poorer HRQOL in long term follow-ups of those with childhood onset epilepsy, a relationship that persists long after remission is established,
and is more robust than disease-related factors (Baca, Vicrey, Caplan, Vassar, & Berg, 2011). The rate of clinically significant depressive symptoms in our sample (21%) was relatively consistent with previous studies (25%) (Plioplys, 2003), and is particularly concerning due to the 3-fold increase in suicide among people with epilepsy compared to the general population (Christensen, Vestergaard, Mortensen, Sidenius, & Agerbo, 2007). Taken together, this information may be clinically meaningful if timely identification and treatment of individuals with depression lead to better outcomes in HRQOL and reduces risk of self-harm.

Baseline weight status showed moderate but non-significant correlations with concurrent depressive symptoms \( r = .48 \) and quality of life \( r = .40 \). Considering the strength of the correlations, the lack of significance likely reflected the small sample size. The positive relationship between weight status and depressive symptoms was in the expected direction given extant literature suggesting that overweight and obese youth have higher rates of depression than their healthy weight peers (Eremis et al., 2004; Puhl & Latner, 2007). With research also showing that children and adolescents with epilepsy are at increased risk for depression (Plioplys, 2003), it is possible that the combination of these conditions compounds risk. As prevalence rates of clinically elevated depressive symptoms in this sample are similar to those previously reported among youth with epilepsy, our findings do not appear to bear out this concern; however, this was not explicitly tested.

We hypothesized that HRQOL would be negatively associated with weight status in line with extant literature documenting lower HRQOL in obese children compared to healthy weight peers (Doyle, le Grange, Goldschmidt, & Wilfley, 2007; Zeller & Modi,
However, the relationship between HRQOL and weight status in the present study was in the opposite direction, such that increasing weight status was related to better HRQOL. It is possible that the individuals on the lower end of the weight spectrum in our sample may have had poorer disease control or additional medical or neurological comorbidities that increased their susceptibility to both being underweight and experiencing a reduced quality of life. For example, children with refractory epilepsy and comorbid cognitive and physical developmental problems experience high rates of feeding difficulties (e.g., chewing, swallowing, self-feeding) that interfere with nutritional and weight status (Bertoli, Cardinali, Veggioetti, Trentani, Testolin, et al., 2006). If this was true in our sample, lower weight status may have corresponded to more severe medical or neurodevelopmental issues that impacted daily functioning. On the other hand, this finding may be idiosyncratic to this small group of children. It would be important to replicate this finding in larger studies before interpreting the significance of the current results.

Overall, findings from the present study were consistent with the well-established body of literature showing that children with epilepsy have lower quality of life than the normative population (Ingerski et al., 2010; Modi, King, Monahan, Koumoutsos, Morita, et al., 2009). Peer interactions around disease disclosure and barriers to obtaining developmentally expected autonomy negatively impact quality of life in adolescents with epilepsy (McEwan et al., 2004). Other factors which have been shown to adversely impact HRQOL in this population include seizure frequency (Camfield, Breau, & Camfield, 2001; Sabaz, Cairns, Bleasel, Lawson, Grinton, et al., 2003) and AED side effects (Benavente-Aguilar, Morales-Blanquez, Rubio, & Rey, 2004; Modi et al., 2011).
Our examination of factors related to quality of life were restricted to AED type and weight status in the present study, and it is a limitation that we could not assess the influence of disease or treatment factors on HRQOL due to the small sample size. In particular, this line of investigation may have shed light on the confusing relationship found between weight status and HRQOL.

The only group differences in psychosocial functioning at either time point was that the weight positive group had significantly worse HRQOL at baseline than the non-weight positive group. This could not be explained by weight status as predicted, since the groups did not differ in BMI z-scores at baseline or over time. However, group differences did exist in the prevalence of developmental delay. Eighty-six percent of the children in the weight positive group had been diagnosed with a developmental delay compared to only 29% in the non-weight positive group. Neuropsychological functioning has been inversely associated with psychosocial functioning among children with epilepsy (Baca et al., 2011; Leonard & George, 1999), and the presence of a developmental delay has been demonstrated to have global negative impacts on quality of life, and particularly adverse effects on social and school functioning (Modi et al., 2009). The greater prevalence of developmental delays among children in the in the weight-positive group may therefore help to explain why they were reported to have lower HRQOL at baseline than those in the non-weight positive group; however, the fact that this difference disappears over time despite the chronic nature of developmental problems weakens this hypothesis.

**Limitations**

This study had several notable limitations. First, the small sample size and imbalance in groups reduced the ability to detect significant findings and precluded
more sophisticated statistical analyses (e.g., structural equation modeling to assess mediation). Beyond recruiting a larger sample, ensuring balance between groups during the recruitment phase will be important for future studies to better assess for AED-related patterns in health behaviors. Additionally, we controlled for age, race, and gender given their established relationship to health behaviors (Odgen et al., 2012; Spear et al., 2007). Given our small sample size, we were unable to look at health behavior patterns by age group. As children age they have more control over their environment and therefore their health behaviors may be more responsive to changes in appetite or energy (e.g., they have increased independent access to food) compared to children whose intake or physical activity is more closely monitored by parents. It would be advisable to explore these as predictors of unhealthy weight status in future studies rather than control for them, as they may help to identify individuals at higher risk who would be more likely to benefit from preventative interventions.

Existing literature suggests that increased weight velocity often occurs within in the first 6 months of AED initiation then stabilizes for the duration of treatment (Demir & Aysun, 2000; Egger & Brett, 1981; Novak et al., 1999). Our sample included many children who have been on AEDs for several years, dramatically reducing our ability to ascertain the impact of initial treatment on changes in growth velocity and consequently insight into causal mechanisms. Effect sizes for group differences in weight status and behavioral health factors were uniformly small and likely reflected, at least in part, the lengthy time since diagnosis. The ideal study would target individuals at epilepsy diagnosis and follow them over the first year of treatment to determine whether AED
initiation in fact produces changes in dietary intake and physical activity that explain accelerated weight gain.

A few individuals in the study were taking stimulant medications for ADHD, a common comorbidity in pediatric epilepsy (Salpekar & Dunn, 2007). These types of medications are known for their appetite suppressing properties (Sonuga-Barke, Coghill, Wigal, DeBacker, & Swanson, 2009) and therefore are a confounding factor. Given the small sample size of the present study, it was not possible to control for stimulant medication. It remains unknown how these medications interact with AEDs to influence dietary intake and weight status.

The questionnaires used to assess psychosocial functioning were parent report. The choice to use parent proxy was deliberate given the high rate of developmental delays among youth with epilepsy that prevented some children from being able to fill out their own measures. Depression is an internalizing condition and may be under-recognized by caregivers compared to externalizing problems. Similarly, the quality of life measure asks parents to subjectively assess their child’s functioning across a range of domains. While physical functioning may be more overtly observed in daily interactions, difficulties in social or emotional functioning may be less apparent to outside observers or have less opportunity to be witnessed, especially as children get older (Eiser & Morse, 2001). Comparison of parent and child reports of HRQOL indicate that parents tend to endorse a lower HRQOL than their children (Baca et al., 2010; Verhey, Kulik, Ronen, Rosenbaum, Lach et al., 2009). HRQOL in pediatric epilepsy is also influenced by parents’ own psychological health (Williams, Steel, Sharp, DelosReyes, Phillips et al., 2003), which was not assessed in our study.
Our sample was heterogenous in terms of seizure etiology, type, and control. While this is positive for generalization to the greater epilepsy population it also makes interpreting results confusing as these factors may interact with medication to produce variability in side effect profiles, behavioral health factors, and psychosocial functioning. Future investigations with more homogenous samples might provide some clarification on these issues or identify a subgroup that would benefit the most from obesity intervention. For example, idiopathic epilepsies (e.g., absence, benign rolandic) have the best prognosis in terms of long-term medical and psychosocial functioning (Shinnar & Pellock, 2004), but have also been associated with the highest rates of overweight and obesity (Daniels et al., 2009). Obesity as a comorbidity for these children may consequently be perceived as more impairing if it compromises their relatively high levels of functioning. Furthermore, a small proportion (14%) of the youth in our study was on polytherapy. This introduces a confound as to whether interactions between medications differentially affect health behaviors (e.g., a weight positive and weight neutral drug wash out changes in appetite). Our inclusion of those individuals is consistent with other studies assessing the impact of AEDs on weight status, especially among newer AEDs that are often tested as add-ons (Biton, 2003b), and is a limitation of the broader literature. On the other hand, polytherapy is common among youth with intractable epilepsy and so understanding the impact of medications both in isolation and in combination is clinically relevant.

Finally, our hospital is a large tertiary care center with a wide catchment area. The distance to treatment likely impacted our study in two significant ways. First, many individuals from farther away opted to complete the follow-up via mail which meant that
we were unable to verify objective measures of height and weight. Secondly, updated information (e.g., medication, comorbidities) was not available in their medical charts.

**Summary**

In closing, our study was the first to assess the role of behavioral health factors in AED induced weight gain among children with epilepsy. While methodological issues limited our ability to properly assess how dietary intake and physical activity related to weight status change during initial medical treatment when AED induced accelerations in growth velocity occur, information gleaned here is still important in documenting behaviors that are related to overall physical and psychosocial health. Future studies in larger samples targeting youth at diagnosis will be better able to elucidate the contribution of health behaviors as potentially explanatory mechanisms in the pathogenesis of AED induced weight gain. Our study was also important in highlighting the high prevalence of overweight/obesity as a comorbidity in this population, along with elevated rates of neurodevelopmental disorders, depressive symptoms, and impaired quality of life compared to healthy peers. Continued efforts to understand the etiology of these issues in combination with the development of evidence-based interventions to mitigate these difficulties will be imperative to promote the best medical and psychosocial outcomes in this highly vulnerable population.
APPENDIX
MEASURES

Parent Measures

Information about your Family

1. Child’s gender (please circle): Male / Female

2. Child’s race (please circle):
   Caucasian  African American  Asian American
   Hispanic    Bi-racial        Other (please specify):_________________

3. Child’s age: ________

4. Child’s Date of Birth: _____/_____/_____

5. Child’s grade in school: _______

6. Your (Parent) Gender (please circle): Male / Female

7. Your race (please circle)
   Caucasian  African American  Asian American
   Hispanic    Bi-racial        Other (please specify):_________________

8. You are the child’s (please select one):
   Mother    _____            Father _____
   Step-Mother _____          Step-Father _____
   Grandparent _____          Other Legal Guardian _____

9. Your (parent/guardian’s): Age_____ Height_____ Weight_____  

10. Please indicate your current living arrangement/marital status (please check one):
   Currently Married _____  Single, Co-Habitating _____
   Single, Divorced _____   Single, Widowed _____
   Single, Never Married _____
11. Including yourself, how many adults live in your home: ________________

12. Including your child, how many children live in your home: ________________

13. What is the highest level (grade) of school you completed?
   - Middle school
   - Some high school
   - Graduated high school
   - Some college
   - Graduated college
   - Post-Graduate school

14. What is your current occupation:
   __________________________________________

15. Estimated Family Income per Year (please check one).
   - Below $9,999
   - $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
   - Over $80,000
Parent’s Medical History

1. Has a doctor ever told you that you have a heart condition and you should only do physical activity recommended by a physician?
   Yes_____ No_____
   If yes, please specify: __________________________________________
   __________________________________________

2. Did a doctor ever say that you had hypertension or high blood pressure? *(Not including high blood pressure only when you were pregnant.)*
   Yes_____ No_____
   If yes, please answer the following:
   a. Did you ever take pills for high blood pressure? Yes_____ No_____
   b. Do you now take pills for high blood pressure? Yes_____ No_____

3. Did a doctor ever say that you had diabetes or high blood sugar? *(Not including diabetes only when you were pregnant.)*
   Yes_____ No_____
   If yes, please answer the following:
   a. Did you ever take pills or insulin for diabetes? Yes_____ No_____
   b. Do you now take pills for diabetes? Yes_____ No_____
   c. Do you now take insulin for diabetes? Yes_____ No_____

4. Are you currently participating in another weight control program?
   Yes_____ No_____
   If yes, please list the name of the program(s) below:
5. Have you previously undergone bariatric surgery?  
   Yes____  No____

6. If you are a female, please answer the following questions:
   a. Are you currently pregnant?  Yes____  No____
   b. Do you plan on becoming pregnant within the next year?  Yes____  No____

7. Has you ever been diagnosed with a depression, bipolar disorder, an anxiety disorder, schizophrenia or mental illness?  
   Yes____  No____
   a. If yes, please specify:

8. Are you currently taking any medications?  
   Yes____  No____
   a. If yes, please list the medications below:

9. How would you describe your weight
   □ Very underweight
   □ Slightly underweight
   □ About right
   □ Slightly overweight
   □ Very overweight
Child’s Medical History

1. Has a doctor told you that your child has any of the following conditions (please mark yes or no for each condition).
   a. Epilepsy
      Yes_____ No _____
   b. Chronic lung disease that limits physical activity
      Yes_____ No _____
   c. Osteoporosis (weak, thin, or brittle bones)
      Yes_____ No _____
   d. Bone or muscle injury that limits physical activity
      Yes_____ No _____

2. Did a doctor ever say that your child had diabetes or high blood sugar? Yes_____ No _____
   If yes, please answer the following:
   a. Did your child ever take pills or insulin for diabetes?
      Yes_____ No _____
   b. Does your child now take pills for diabetes?
      Yes_____ No _____
   c. Does your child now take insulin for diabetes?
      Yes_____ No _____

3. Has a doctor ever told you that your child had heart problems? Yes_____ No _____
   If yes, please answer the following questions:
   a. Heart valve problems (tight or narrowed valves or leaky valves)
      Yes_____ No _____
   b. Heart valve surgery (artificial valve or repair of valve)
      Yes_____ No _____
   c. Atrial fibrillation (irregular beating of the heart requiring pills for treatment)
      Yes_____ No _____
   d. If other, please describe:
      ______________________________________________________________
      ______________________________________________________________
      ________________________________
      ________________________________
      ______________________________________________________________
      ______________________________________________________________
      ______________________________________________________________
      ______________________________________________________________

76
4. Did a doctor ever say that your child had/has hypertension or high blood pressure?
   Yes____  No_____

   If yes, please answer the following questions:
   a. Does your child currently take pills for high blood pressure?  Yes____  No _____

5. Has your child ever been diagnosed with a developmental delay, autism, bipolar disorder, childhood schizophrenia or other major psychiatric disorder?
   Yes____  No_____
   a. If yes, please specify:  
       _________________________________________________________________
       _________________________________________________________________

6. Is your child currently taking any medications?
   Yes____  No_____
   a. If yes, please list them below:  
       _________________________________________________________________
       _________________________________________________________________

7. How would you describe your child’s weight?
   □ Very underweight
   □ Slightly underweight
   □ About right
   □ Slightly overweight
   □ Very overweight

8. In terms of overall health, how concerned are you about your child’s weight?
   □ Not concerned
   □ A little concerned
   □ Concerned
   □ Very concerned
9. Currently, how frequently does your child have seizures?

- Multiple times per day
- Daily
- Weekly
- Monthly
- Yearly
- Less than once per year
Chart Review and Administrative Forms

ACCELEROMETRY and ANTHROPOMETRIC DATA

Participant ID#: __________________ Date:__________________

Instructions:
This form is completed by a staff member. Please interview the participant to obtain the relevant information.

Staff member’s name: ______________________________

1. Staff member, please complete the following questions as indicated:
   a. What is the child’s Date of Birth? __________________
   b. What is the child’s Gender
      ☐ Male ☐ Female
   c. Child’s Weight (kg): (measure 3 times)
      1:________
      2:________
      3:________
   d. Child’s Height (cm): (measure 3 times)
      1:________
      2:________
      3:________
   e. Which hand does child write with?
      ☐ LEFT ☐ RIGHT
   (Before asking the next question, inquire as to whether child has experimented with smoking. Then ask whether they currently smoke regularly. Check YES if child is currently a regular smoker.)
   f. Is child currently a smoker?
      ☐ YES ☐ NO

Notes:
________________________________________________________
________________________________________________________
________________________________________________________
________________________________________________________
Retrospective Medical Chart Review

Study ID: _____________________________________________

Date of epilepsy diagnosis: _____________________________

Seizure Type: _________________________________________

Baseline Visit

Date: _____________                   Child Height: _________

Child weight: __________

Comorbid Medical Diagnoses
1) Dx: ______________________________________________
2) Dx: ______________________________________________
3) Dx: ______________________________________________
4) Dx: ______________________________________________
5) Dx: ______________________________________________

Psychiatric Diagnoses
1) Dx: ______________________________________________
2) Dx: ______________________________________________
3) Dx: ______________________________________________

Medications
1) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ __
   Date of termination: _________
   Reason for termination: ______________________________________________

2) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ ___
   Date of termination: _________
   Reason for termination: ______________________________________________

3) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ ___
   Date of termination: _________
   Reason for termination: ______________________________________________

4) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ ___
   Date of termination: _________
   Reason for termination: ______________________________________________

5) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ ___
   Date of termination: _________
   Reason for termination: ______________________________________________

6) Name: _______________________
   Dosage: _______________________
   Date of initiation: __________ ___
   Date of termination: _________
Reason for termination: ______________________________________________________
Prospective Medical Chart Review

Study ID: ___________________________

Prospective Visit 1 (approximately 4-6 months post-baseline)

Date: _____________                   Child Height: _________                Child weight: __________

Comorbid Medical Diagnoses
  6) Dx: __________________________________
  7) Dx: __________________________________
  8) Dx: __________________________________
  9) Dx: __________________________________
 10) Dx: _________________________________

Psychiatric Diagnoses
  4) Dx: __________________________________
  5) Dx: __________________________________
  6) Dx: __________________________________

Medications

  7) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________

  8) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________

  9) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________

10) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________

11) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________

12) Name: ______________________________ Dosage: __________________
     Date of initiation: ___________ ___ Date of termination: __________
     Reason for termination: __________________________________________
LIST OF REFERENCES


Varni, J.W., Seid, M., & Kurtin, P.S. (2001). PedsQL(TM) 4.0: Reliability and Validity of the Pediatric Quality of Life Inventory(TM) Version 4.0 Generic Core Scales in Healthy and Patient Populations. *Medical Care, 39*(8), 800-812.


BIOGRAPHICAL SKETCH

Katherine Wells Follansbee-Junger graduated Summa Cum Laude from the University of Vermont with a Bachelor of Arts in psychology. Following a 3-year post-baccalaureate position at Brown University, she came to the University of Florida to study pediatric psychology. She received her Ph.D. in clinical psychology in the summer of 2012.