ABSTRACT

The Relationship Between Subjective Cognitive Complaints and Objective Cognitive Measures in the Epilepsy Clinic: An Exploratory Study of the Neuro-QOL Subjective Cognition Measures

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One of the most consistently distressing symptoms for patients with epilepsy and psychogenic non-epileptic events (PNEE) is cognitive dysfunction (Meneses, Pais-Ribeiro, da Silva & Giovagnoli, 2009). Deficits in cognitive domains such as memory, language, and executive functioning contribute to a decreased quality of life in both patients with epilepsy and those with PNEE (Meneses et al., 2009). There is evidence of an association of cognitive complaints in patients with epilepsy and PNEE, but the relationship between subjective cognitive complaints and objective cognitive deficits is currently unclear (Giovagnoli, 2013). The current study explored the relationship between subjective cognitive complaints and objective cognitive measures through analysis of retrospective data collected at an epilepsy clinic. Data from thirty-nine

patients diagnosed with either epilepsy, PNEE or PNEE with comorbid epilepsy were reviewed. Results did not reveal any significant relationships between subjective cognitive complaints and objective cognitive impairment in any of the cognitive domains assessed (memory, visual skills, language, attention/working memory, executive functioning, and processing speed). Additionally, subjective measures of cognition demonstrated high sensitivity but low specificity for objective cognitive deficits across the different domains of cognition. Depression emerged as a significant predictor of subjective cognitive complaints over and above other predictors such as anxiety and objective measures of cognition. A secondary, exploratory analysis found no significant difference between diagnostic groups in terms of the relationships between subjective cognitive complaints and objective cognitive deficits. The results suggest that subjective cognitive complaints should be interpreted cautiously as measures of cognition in this population.

The Relationship Between Subjective Cognitive Complaints and Objective Cognitive Measures in the Epilepsy Clinic: An Exploratory Study of the Neuro-QoL Subjective Cognition Measures

by

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DEDICATION

To my parents: I would not be the person I am today without your support and love.

To Ned, Kim, and Lizzy: I could not have survived graduate school with my mental health intact without your friendship.

CHAPTER ONE

Introduction

Background

Subjective cognitive complaints are common in neurological conditions and can have significant impact on patients' quality of life and day-to-day functioning (Kobau et al., 2014; Mitchell, Kemp, Benito-León, & Reuber, 2010). The prevalence of these complaints and the significance of their impact on patients' biopsychosocial functioning have prompted the National Institute of Health (NIH) and the National Institute of Neurological Disorders and Stroke (NINDS) to incorporate cognitive complaints into the Patient Reported Outcomes Measurement Information System (PROMIS) and Neuro-QOL (Cella et al., 2011; Nowinski et al., 2010; Reeve et al., 2007). Both the PROMIS and Neuro-QOL are brief, psychometrically sound assessment systems that assess for a range of relevant domains in patient-reported, health-related quality of life. The two systems share a large degree of conceptual overlap and some item overlap (Nowinski et al., 2010; Reeve et al., 2007). Both include scales to assess for patient perceived cognitive functioning in addition to many other domains of functioning (Nowinski et al., 2010, Reeve et al., 2007). The development of these two measures is partially driven by a weakness in clinical research, where there is little standardization in the measures used to assess progress and outcome of various symptoms across conditions (Nowinski et al., 2010). The PROMIS and Neuro-QOL assessment systems allow for better cross-disease and cross-study comparisons of the various health-related quality of life domains as a

function of various treatments or other factors (Cella et al., 2011; Nowinski et al., 2010). The flexibility in administration and ease of individualization of these measures makes them ideal for use in medical or other clinical settings for the purposes of screening, monitoring treatment progress, and quality of care (Nowinski et al., 2010). By creating a common language for researchers and clinicians across diseases and studies, the PROMIS and Neuro-QOL assessment systems can not only further research but also begin to close the gap between research and clinical application that exists today.

The Neuro-QOL has identified epilepsy as one of their target populations for studying these new instruments due to its prevalence and associated personal and societal costs which clinicians and researchers alike are attempting to ameliorate (Elliott & Richardson, 2014; Cella et al., 2011). Epilepsy affects approximately 2.2 million adults and children in the United States, with 150,000 new cases annually (Institute of Medicine report, 2012). It is the fourth most common neurological disorder in the United States, and estimates suggest direct and indirect costs exceeding $12.5 billion annually (Institute of Medicine report, 2012; Begley et al., 2000). Both adults and children with epilepsy symptoms that are more difficult to control tend to incur more costs and more comorbid disorders as compared to those with more manageable epilepsy symptoms (Cramer et al., 2014; Wilner, Sharma, Thompson, Soucy & Krueger, 2014). In terms of social impact, studies demonstrate that there are higher unemployment rates, earlier retirement rates, lower marriage rates, and higher perception of stigma among patients with epilepsy as compared to both healthy populations and individuals with other neurological disorders (Aydemir, Özkara, Ünsal & Canbeyli, 2011; Marinas et al., 2011; Smeets et al., 2007). Seizure severity, lowered self-efficacy, and lack of social support are all factors that may

contribute to the social impact of the disorder (Elliot & Richardson, 2014; Quintas et al., 2012; Elliott, Charyto, Sprangers, Lu & Moore, 2011; Marinas et al., 2011; Smeets et al., 2007). While epilepsy impacts many aspects of an individual's life, one of the most consistently distressing symptoms to patients is cognitive dysfunction (Meneses, Pais-Ribeiro, da Silva & Giovagnoli, 2009; Piazzini, Beghi, Turner, Ferraroni & LICE Quality of Life Group, 2008; Pais-Ribeiro, da Silva, Meneses & Falco, 2007; Giovagnoli & Avanzini, 2000).

Objective Cognitive Difficulties in Epilepsy

Cognitive deficits as measured by neuropsychological tests are common in the epilepsy population (Schoenberg, Werz, & Drane, 2011; Motamedi & Meador, 2003) and can occur across a wide range of cognitive domains (Schoenberg et al., 2011; Motamedi & Meador, 2003). These difficulties seem to be associated with biological factors (e.g. location of seizure focus, extent of underlying neurological damage), seizure-related factors (e.g. type, frequency), treatment-related factors (e.g. medications, surgery), and psychosocial factors (e.g. depression and anxiety; Korczyn et al., 2013; Motamedi & Meador, 2003). In terms of biological factors, while the type of seizures is not predictive of the severity of cognitive impairment, the location of the seizure focus in the brain has been shown to be correlated with particular domains of cognitive dysfunction (Rudzinski, 2013; Tramoni et al., 2010; Meador, 2002). As neurobiological substrates for cognition directly affect objective cognitive impairment, it's reasonable to assume that seizure variables that impact neurobiological substrates also correlate with specific cognitive deficit (Marquez et al., 2007; Fuerst et al., 2003). For example, Fuerst and colleagues (2003) demonstrated that temporal lobe epilepsy is correlated with hippocampal volume

loss and memory impairment. Other seizure-related factors implicated in cognitive impairment include seizure duration, frequency, and treatments for seizures such as antiepileptic drugs (Rudzinski, 2013; Helmstaedter et al., 2003).

Additionally, there is evidence that psychological factors such as depression and anxiety also negatively impact cognitive functioning in epileptic populations (Rösche, Kundt, Weber, Fröscher, & Uhlmann, 2012; Busch et al., 2011; Mula & Trimble, 2009). Specifically, there is evidence that high levels of depression and anxiety are correlated with and predictive of cognitive impairment (Brown et al., 2014; Busch et al., 2011). Regardless of the etiology of these cognitive deficits, cognitive dysfunction has been consistently shown to be correlated with a negative quality of life in this population and remains an important area to explore (Meneses et al., 2009; Piazzini, et al., 2008; Pais-Ribeiro et al., 2007; Giovagnoli & Avanzini, 2000).

Subjective Cognitive Complaints in Epilepsy

In addition to measurable cognitive deficits, there is also ample evidence of subjective cognitive complaints in the epilepsy population as compared to healthy controls (Rayner, Wrench, & Wilson, 2010; Prigatano & Kirlin, 2009; Baños et al., 2004; Elixhauser, Leidy, Meador, Means, & Willian, 1999; Giovagnoli, Mascheroni, & Avanzini, 1997). The majority of the literature has focused on memory complaints as those are one of the most common concerns among this population and significantly decrease quality of life (Fargo et al., 2004). Some of the most common complaints include being unable to remember a joke, experience, or story; “tip of the tongue” experience; and forgetting names of people met during social occasions (Hendriks, Aldenkamp, van der Vlugt, Alpherts, & Vermeulen, 2002). These complaints are not

limited to specific epilepsies and their severity can vary across the same types of epilepsy (Giovagnoli et al., 1997; O'Shea et al., 1996). Seizure frequency, antiepileptic drug regimen, and psychological factors such as depression and anxiety are other factors that have been associated with subjective memory complaints (Giovagnoli, 2013; Rayner et al., 2010, Marino et al., 2009; Uijl et al., 2006; Baños et al., 2004; Piazzini et al., 2001; Elixhause et al., 1999). While there is robust evidence of the effect that mood, epilepsy-related factors, and antiepileptic drug regimen can have on subjective cognitive complaints, their relationship with objective cognitive impairment is less clear.

Relationship between Subjective and Objective Cognitive Measures in Epilepsy

While both objective cognitive deficits and subjective cognitive complaints are common in epilepsy, surprisingly, the relationship between these two is unclear (Witt, Glockner, & Helmstaedter, 2012; Hall, Isaac, & Harris; 2009; Baxendale & Thompson, 2006; Piazzini, Canevini, Maggiori, & Canger, 2001). This raises the question as to what subjective cognitive complaints actually signify. Without a clear understanding of this relationship, the utility of subjective cognitive complaints greatly decreases for a clinician (Fargo et al., 2004).

The majority of the work examining the relationship between objective deficits and subjective complaints in epilepsy populations has centered on memory (Witt et al., 2012; Rayner et al., 2010; Hall et al., 2009; Fargo et al., 2004). To this end, there are a number of studies that reported small to moderate relationships between subjective memory complaints and objective memory measures (Witt et al., 2012; Rayner et al., 2010; Hall et al., 2009; Au et al., 2006; Fargo et al., 2004; Lineweaver et al., 2004; Elixhauser et al., 1999; Giovagnoli et al., 1997). There was no specific subdomain of

objectively assessed memory (e.g. visuospatial memory, retrieval ability, verbal memory) that consistently predicted or correlated with subjective memory complaints. In particular, Giovagnoli and colleagues (1997) looked at 100 patients with various epilepsy diagnoses and demonstrated that delayed visual memory recall was significantly correlated with and predictive of subjective memory complaints. Other studies have yielded similar results, where there existed small to moderate correlations between subjective memory complaints and objective visual memory measures (Rayner et al., 2010, Elixhauser et al., 1999). This relationship between subjective and objective memory may also exist longitudinally. Lineweaver and colleagues (2014) assessed for objective and subjective measures of memory in a sample of epilepsy patients who underwent surgery to treat their seizure disorders pre and post-surgery. Results indicated that patients whose objective memory ability had declined post-surgery demonstrated a parallel decrease in their reported memory ability post-surgery relative to pre-surgery (Lineweaver et al., 2014).

Another common objective memory factor with significant associations to subjective memory functioning is verbal recall and language. Six studies reported significant associations between subjective memory complaints and either short-term verbal memory retention, long-term memory retrieval, or overall language ability (Witt et al., 2012; Rayner et al., 2010; Au et al., 2006; Fargo et al., 2004; Elixhauser et al., 1999; Giovagnoli et al., 1997). Other cognitive domains, though not as frequently explored, may also be correlated with subjective cognitive complaints. For example, Fargo and colleagues (2004) demonstrated a small but significant correlation between objective verbal memory and subjective ratings of attention/concentration. More recently, a study

in the pediatric epileptic population yielded results demonstrating a small correlation between processing speed and perceived cognitive function in the pediatric Neuro-QOL (Lai et al., 2015). Clearly, there is emerging evidence of some relationship between some domains of cognitive impairment and subjective cognitive complaint. However, in all of the studies, the percent of variance explained by objective memory measures was small to moderate, suggesting this to be an area worth further exploration and that other variables may be related to these complaints.

While some studies have demonstrated significant relationships between subjective cognitive complaints and objective cognitive measures, numerous others have found no relationship, or overestimation or underestimation of objective cognitive deficits (Liik, Vahter, Gross-Paju, & Haldre, 2009; Prigatano & Kirlin, 2009; Baxendale & Thompson, 2005; Baños et al., 2004; Fargo et al., 2004; Jungwirth et al., 2004; Piazzini, Canevini, Maggiori, & Canger, 2001). Fargo and colleagues (2004) assessed the objective and subjective cognitive ability of 193 patients in the epilepsy monitoring unit and discovered no substantial relationship between these two variables. The results indicated that patients in the epileptic group had tendencies to overestimate both language and attention/concentration abilities (Fargo et al., 2004). These results also hold true for patients with generalized and partial epilepsies (Liik et al., 2009; Piazzini et al., 2001), elderly adults with no evidence of dementia but with diagnosis of epilepsy (Jungwirth et al., 2004), and patients who've undergone surgery for intractable epilepsy (Baños et al., 2004). While Piazzini and colleagues (2001) demonstrated that epileptic patients underestimated memory performances, results from Liik and colleagues (2009) suggest that there is a trend for negative correlations between objective cognitive functioning

measures and subjective cognitive complaints. In other words, patients with better neuropsychological functioning tend to report more self-reported problems and vice versa (Liik et al., 2009). Overall, there is a lack of consistency in the direction of discordance between the various domains of cognitive functioning and subjective cognitive complaints (Giovagnoli, 2013).

One of the reasons cited for the discrepancy between objective and subjective measures of cognition in epileptic patients is the disparity of the memory constructs that objective and subjective instruments assess (Giovagnoli, 2013; Hall et al., 2009). For example, a subjective memory measure may ask how often names, faces, dates, or forgetting what to buy at the store occurs and their level of impact, but objective memory measures assesses for recall of stories, words, or figures over 30 minutes or longer. Memory measures that have higher ecological validity, or resemble more everyday memory tasks, have been shown to have higher correlations with subjective memory measures (Grewe et al., 2014; Hall et al., 2009; Elixhauser et al., 1999).

Another area that dominates the literature addressing the discrepancy between subjective and objective memory functioning is the effect of emotional factors such as depression and anxiety. Numerous studies have found that self-reports of anxiety and depression are highly correlated with and predictive of subjective memory functioning (Giovagnoli, 2013; Rayner et al., 2010; Liik et al., 2009; Marino et al., 2009; Au et al., 2006; Baños et al., 2004; Piazzini et al., 2001; Elixhauser et al., 1999). In studies where the authors demonstrated small to moderate relationships between subjective and objective memory, the results also indicate that the associations between subjective memory and depression or anxiety are consistently larger (Au et al., 2006; Piazzini et al.,

2001; Elixhauser et al., 1999). Baños and colleagues (2004) examined the relationship between mood and subjective memory complaints in epilepsy patients who have undergone surgery as part of their treatment and reported that emotional factors were able to better predict subjective memory complaints than any objective cognitive measure across all cognitive domains assessed. There is strong support in the literature for a relationship between emotional functioning and subjective cognitive functioning. Other factors that have been attributed to the difference between subjective and objective memory measures include polytherapy of antiepileptic drugs and other seizure-related factors (Hall et al., 2009; Salas-Puig et al., 2009; Uijl et al., 2006). Clearly, the relationship between subjective and objective cognitive performance in epilepsy is complex and the PROMIS and Neuro-QOL cognitive measures will require similar close study to determine their relationship to cognitive constructs in epilepsy.

There are several limitations amongst these studies. One of the most important limitations is a lack of consistency in the assessments used for objective and subjective measures of memory (Witt et al., 2012; Rayner et al., 2010; Elixhauser et al., 1999). Studies range from using a few scales to assess for specific domains of memory functioning (Piazzini et al., 2001) to a full battery of neuropsychological measures (Fargo et al., 2004) with few tests in common. While each study provides valuable insight individually, having standardized measures for both subjective and objective measures of cognition would allow for easier and more meaningful comparisons across studies and across disorders, which would help streamline research within the field. Another limitation is population specificity for particular epilepsy diagnosis, which can limit the generalizability of the results (Rayner et al., 2010; Jungwirth et al., 2004; Lineweaver et

al., 2004). There were also methodological flaws in some studies. For example, Au and colleague's study (2006) relied on self-report for seizure rates and seizure types, which may decrease the validity of some of the results relating to seizure-related variables. Lastly, while memory constitutes one of the chief complaints and problems in the epilepsy population, one of the weaknesses in the current literature lies in the lack of expansion to other cognitive domains. As noted above, there is evidence that cognitive deficits can occur in a host of different cognitive domains such as visual or verbal processing, executive functioning, or attention, yet studies to date have not thoroughly explored these domains of subjective cognitive functioning. Currently, the preponderance of self-report measures of cognition assess subjective memory abilities.

Psychogenic Non-Epileptic Events (PNEE)

As complex as the relationship between subjective and objective cognitive difficulties in epilepsy is, for practicing clinicians, another important constituency in epilepsy clinics is individuals with psychogenic non-epileptic events (PNEE). Studies cite the prevalence of PNEE patients as between 5% and 10% of outpatients in epilepsy clinics and 20% to 40% of inpatients in epilepsy monitoring units (Asadi-Pooya & Sperling, 2015). Psychogenic non-epileptic events are defined by the presence of behavioral events resembling epileptic seizures accompanied by a lack of electrophysiological correlate on electroencephalograms (Bodde et al., 2009; Reuber & Elger, 2003). The population incidence of PNES has been estimated at approximately 1.5/100,000 persons per year although the difficulty in differential diagnosis of PNEE strongly suggests these numbers to be an underestimate of the actual incidence level (Baslet, 2011; Reuber & Elger, 2003). The etiology of PNEE is not well-understood.

While there is dissent in the literature on the specific psychological factors that underlie and produce the symptomology of PNEE, there is agreement that the seizure symptoms of PNEE are propagated and are a result of psychological and emotional dysfunction and dysregulation (O'Brian et al., 2015; Bodde et al., 2009; Reuber & Elger, 2003).

Currently, the gold-standard for the differential diagnosis of PNEE is video-electroencephalogram (video-EEG), which simultaneously records brainwaves through EEG and a video of the patient during the recording (Bettini, Croquelois, Maeder-Ingvar, & Rossetti, 2014). While video-EEG is effective at differentiating between PNEE and epilepsy, the difficulty in differentially diagnosing PNEE contributes to the long retention period between initial symptom manifestation and accurate diagnosis, which can cause undue financial and psychological burden for the patients (Ahmedani et al., 2013; Whitehead, Kandler, & Reuber, 2013; Bodde et al., 2009; Fiszman, Alves-Leon, Nunes, D'Andrea & Figueira, 2004; Reuber & Elger, 2003). This is further complicated by patients who demonstrate both PNEE and epilepsy symptoms (Herskovitz, 2015). Few studies have directly studied the prevalence of the subpopulations of PNEE patients who also present with epilepsy. The studies that have previously reported on prevalence of PNEE and epilepsy have had dubious criteria for this categorization (Benbadis, Agrawal, & Tatum, 2001). Benbadis and colleagues (2001) examined the prevalence and found that slightly less than 10% of patients with PNEE displayed evidence of epilepsy. The distinction of diagnosis between epilepsy, psychogenic non-epileptic events and psychogenic non-epileptic events with comorbid epilepsy is vital because of its impact on treatment recommendations, particularly when some of the viable options for treatment include invasive procedures such as surgery or medications with significant side effects

(Benbadis et al., 2001). Moreover, much less is understood about this mixed population as it is often excluded from studies looking at epileptic and nonepileptic seizure populations due to the complications they may introduce to the data (Myers et al., 2012; Fargo et al., 2004; Szaflarski et al., 2003). Similar to epilepsy, there is robust evidence demonstrating a decreased health-related quality of life for patients with PNEE compared to not only healthy controls, but also to epilepsy populations (Karakis et al., 2014; Akdemir et al., 2013; J. Szaflarski & M. Szflarski, 2004; Szaflarski et al., 2003).

Objective Cognitive Decline in PNEE

While a psychological etiology is suspected for PNEE, objective cognitive impairments are not uncommon in this population (O'Brien et al., 2015; Gul & Ahmad, 2014; Hill & Gale, 2011; Strutt, Hill, Scott, Uber-Zak, & Fogel, 2011; Reuber, 2008; Reuber, Fernández, Helmstaedter, Quirshi, & Elger. 2002; Kalogjera-Sachellares & Sackellares, 1999). The domains of cognition affected are varied across studies and included language, attention, executive functioning, memory, visual-motor speed, and working memory (O'Brien et al., 2015; Gul & Ahmad, 2014; Hill & Gale, 2011; Strutt et al., 2011; Reuber, 2008; Reuber et al., 2002; Kalogjera-Sackellares & Sackellares, 1999).

There is inconsistent evidence in comparing performance on objective cognitive measures between PNEE and epileptic populations. While some studies have demonstrated small, significant differences in scores on neuropsychological assessment measures between PNEE populations and epilepsy populations (Hill & Gale, 2011; Drane et al., 2006; Breier et al., 1998; Binder, Salinsky, & Smith, 1994), most studies have found no such difference in performance nor any difference between PNEE populations and populations with comorbid PNEE and epilepsy (Turner et al., 2011; Reuber et al.,

2002; Kalogjera-Sackellares & Sackellares, 1999). Thus far, researchers have been unable to identify a pattern of cognitive deficits specific to either the PNEE or PNEE with epilepsy populations. The etiology of these cognitive deficits is also unclear and particularly puzzling as there is little biological underpinning for cognitive deficits as compared with epilepsy populations (Baslet, 2011; Schoenberg et al., 2011). Current hypotheses propose that the presence, or history, of neurobiological injuries or intervening variables such as pain, fatigue, anxiety, or depression play important roles in decreased cognitive performance in this population (Schoenberg et al., 2011). One limitation in the studies looking at objective cognitive deficit in PNEE populations is small sample size and an inconsistent inclusion criteria of PNEE patients with comorbid epilepsy. While small sample size may decrease the power of the study, variability in the sampling of PNEE populations limits the generalizability of the results to the overall PNEE population, which has already been shown to be diverse (O'Brien et al., 2015; Turner et al., 2011; Bodde et al., 2009).

Subjective Cognitive Complaints in PNEE

Similar to epilepsy, there is evidence of subjective cognitive complaints in the PNEE population. However, this is less well characterized compared to the epileptic populations (Fargo et al., 2004). Studies have found that patients with PNEE tended to report complaints in the domains of memory, attention, concentration, and language (Myers, Lancman, Laban-Grant, Matzner, & Lancman, 2012; Prigatano & Kirlin, 2009; Fargo et al., 2004; Szaflarski et al., 2003; Breier et al., 1998). While some of the studies found significant difference in the scores of subjective cognitive functioning of PNEE versus epileptic populations (Fargo et al., 2014; Szaflarski et al., 2003) across all

cognitive domains, another only found significant differences in either one domain (Prigatano & Kirlin, 2009) or no significant differences between epileptic and PNEE groups (Breier et al., 1998). Regardless of the etiology of subjective complaints in PNEE populations and how they compare against those of epileptic populations, these cognitive complaints have been shown to have small to moderate correlations with decreased quality of life and are therefore an important area of research to expand in (Myers et al., 2012).

Relationship between Subjective and Objective Cognitive Measures in PNEE

There are very few studies that examine the relationship between subjective and objective measures of cognition in the PNEE population (Prigatano & Kirlin, 2009; Fargo et al., 2004). Fargo and colleagues (2004) assessed the subjective and objective measures of verbal memory, language, and attention and concentration in patients diagnosed solely with definitive PNEE. The authors not only compared agreement of objective versus subjective measures of the cognitive domains selected, they also examined the accuracy of the discrepancies (Fargo et al., 2004). The results demonstrated that patients with PNEE were able to accurately rate attention and concentration but underestimated memory and overestimated language abilities. Prigatano & Kirlin (2009) found similar results in their study where they compared subjective and objective cognition measures in both epileptic and PNEE groups. The results showed that PNEE patients underestimated their word-finding difficulty, a task that assesses for language (Prigatano & Kirlin, 2009). While there is inconsistent evidence for the relationship between subjective and objective measures of cognition in the epilepsy population, there is a distinct lack of studies in the

PNEE literature. As PNEE patients may make up 10% to 40% of the population in epilepsy clinics, there is a need for more research in this area.

Summary

Cognitive complaints are common in individuals with epilepsy and PNEE, but there is disagreement as to what exactly these complaints mean in relation to objectively measured cognition. Given that cognitive complaints are related to important outcomes such as health-related quality of life and have been incorporated into patient-reported outcome batteries that are used across populations with a variety of neurological conditions, additional understanding is required regarding the new Neuro-QOL and PROMIS measures in the epilepsy clinic population in order to better clarify and understand the relationship between subjective cognitive complaints and objective cognitive deficits. This study further explored this relationship through correlation and multiple regression analysis of the subjective measures of cognition on the Neuro QOL (Neuro-QOL Applied Cognitions- General Concerns and Neuro-QOL Applied Cognitions- Executive Functioning) and six cognitive domains (visual-skills, language, memory, executive functioning, processing speed, and attention/working memory). Additionally, sensitivity and specificity calculations were utilized to assess the specificity and sensitivity of subjective cognitive complaints for objective cognitive impairment.

Aims of the Study

Aim 1: Explore the relationship between subjective and objective measures of cognition.

H1: There will be small to moderate correlations between the 6 objective cognitive composite scores (language, visual skills, memory, executive functioning, attention/working memory, processing speed) and both the Applied Cognitions – General Concerns score and the Applied Cognitions – Executive Functioning score.

Aim 2: Explore the specificity and sensitivity of subjective cognitive complaints to objective cognitive measures.

H2: Subjective cognitive complaint measures will have high sensitivity but low specificity to measured cognitive impairments.

ROC curves will be utilized to determine what, if any, is the optimal cut point for subjective cognitive complaints to predict impairment in cognitive functioning.

Aim 3: Explore depression and anxiety as predictors of subjective cognitive functioning.

H3: Depression and anxiety will both emerge as significant predictors of subjective cognitive functioning, over and above the predictive ability of objective cognitive variables.

Aim 4: Secondary aims include exploring differences between PNEE, epileptic, and PNEE with comorbid epilepsy groups in terms of the relationship between subjective cognitive complaints and objective cognitive deficits.

H4: It is hypothesized that there will minimal differences in the relationship between subjective cognitive complaints and objective cognitive deficits between PNEE, epileptic groups, and PNEE with comorbid epileptic groups.

CHAPTER TWO

Methods and Materials

Participants

A retrospective review of data collected from referrals from the epilepsy clinic at Baylor Scott and White in Temple, Texas between 12/1/2010 and 12/31/2014 was completed. Cases reviewed were those referred for neuropsychological testing by their treating neurologist after long-term video EEG monitoring or outpatient ambulatory EEG by the epileptologist or neurologist. Inclusion criteria for the current study included completion of the neuropsychological and personality measures pertinent to the study, with non-completers excluded from the analysis. Individuals who were found to have another medical cause for their events (i.e. metabolic imbalance) were excluded. Performance validity measures were administered to all patients, and individuals whose performance suggests invalid responding on either cognitive or personality measures or who scored less than 45 on the TOMM 2 were removed from further analysis. Once the cases were identified, the medical records were accessed to clarify their diagnoses, relevant EEG findings, and neuroimaging findings. Final diagnoses (i.e. epilepsy, PNEE, or PNEE with comorbid epilepsy) were made by a board-certified epileptologist. Data from the neuropsychological evaluations, without any HIPPA identifiers, were coded for further analysis.

Measures

As part of the standard evaluation process for cases referred for the epilpetologists in the BSWH clinic, incoming referrals were administered a core battery of neuropsychological tests, personality measures, and self-reported quality of life measures. The domains of interest to this study include memory, language, attention/working memory, processing speed, executive functioning, and visual skills as well as depression and anxiety.

Each domain was represented by a composite score for a total of 6 composite scores, with two tests comprising each summary measure. Scores for each of the tests or subtests listed below were first transformed into a demographically-adjusted score on the basis of age, gender, education, and/or ethnicity-matched normative data. For the Wechsler family of tests, demographically corrected scores were based on the results of the Advanced Clinical Solutions demographic adjustments (Wechsler, 2009). For the Boston Naming Test and Trail Making Test B, demographic corrections were based on the Expanded Halstead-Reitan Normative database (Heaton, Miller, Taylor, & Grant, 2004). For the Ruff Figural Fluency Test, manual norms were used (Ruff, Rudolph, Light, & Randall, 1987). For this study, impairment was defined as average performance greater than one standard deviation below the mean. Instruments from each domain are described below.

Demographics

The demographic information collected for each individual included gender, age, handedness, years of education, and diagnosis. The final diagnosis of type of epilepsy, PNEE or mixed diagnosis, as noted above, was made by a board-certified epileptologist.

Objective Measures of Cognition

Memory. For this study, memory was defined as delayed free recall of verbal and visual material and measured using a composite score consisting of the Visual Reproduction II subtest of the Wechsler Memory Scales, Fourth Edition (WMS-IV) and the Delayed Recall measure of the California Verbal Learning Test, Second Edition (CVLT-II).

The WMS-IV is a battery designed to assess visual and verbal/auditory memory. For this study, the Visual Reproduction II (VRII) subtest of the WMS-IV was used to assess for visual memory. This subtest requires the individual to view a design and then draw it from memory after a 20- to 30- minute delay (Wechsler, 2009). A test-retest reliability coefficient of .96 has been reported for this subtest (Wechsler, 2009). Visual memory is an important area to assess in epileptic populations and the use of VR II to assess visual memory in epileptic populations is well-established (NINDS CDE Team, 2010; Locke et al., 2006; Fargo et al., 2004).

The Delayed Recall measure of the CVLT-II was used to assess for verbal memory. For the CVLT-II, the individual is asked to memorize a list of 16 words over 5 trials and then asked to recall them after a long delay (Strauss, Sherman & Spreen, 2006). Delayed Recall has demonstrated high test-retest reliability (r = .88) and mostly adequate to high correlations with its predecessor, the CVLT (Strauss, Sherman & Spreen, 2006). Verbal memory has been established as an important area to assess by the National Institute of Neurological Disorders and Stroke (NINDS) Common Data Elements (CDE) for Epilepsy and CVLT is widely used as a test of verbal memory in the epilepsy literature across adults and children (Brown et al., 2014; Hernandez et al., 2003).

Processing speed. The Processing Speed Index (PSI) of the WAIS-IV was used as an assessment of processing speed of visual information. The PSI is a composite measure in the WAIS-IV battery that includes scaled scores from the Digit-Symbol Coding and Symbol Search subtests. The PSI has a reported reliability score of .90 and a moderate to high convergent validity (r = .72) with the Number-Letter Switching Completion Time of the Delis-Kaplan Executive Functioning Scale (D-KEFS), another measure that measures processing speed (Wechsler, 2008). Processing speed is an important area to measure in epilepsy and the PSI is highly recommended and commonly utilized to assess for this domain of cognitive functioning (NINDS CDE Team, 2010; Schoenberg et al., 2011; Velissaris, Wilson, Newton, Berkovic, & Saling, 2009).

Attention/Working memory. The Working Memory Index (WM) of the WAIS-IV was used to assess for attention and working memory. The WM is a composite score that includes scores from the Arithmetic, Digit Span, and Letter-Number Sequencing subtests of the WAIS-IV. The WM has a reported reliability score of .94 and moderate convergent validity (r= .62) with other measures of attention such as the attention score of the RBANS (Wechsler, 2008). Attention and working memory are areas of particular import in epilepsy (NINDS CDE Team, 2010). Although the WM composite score is not commonly used with epileptic populations as a measure of attention and working memory, its subtests often are (Prigatano & Kirlin, 2009; Fargo et al., 2004; Piazzini et al., 2001).

Visual skills. The Perceptual Reasoning Index (PRI) is a composite measure of the WAIS-IV that was used to assess for visuospatial ability. The PRI composite score

includes scaled scores from the Block Design and Matrix Reasoning subtests of the WAIS-IV (Wechsler, 2008) in this case. The PRI has a reported reliability score of .87 and a moderate to high convergent validity (r = .66) with the Visuospatial/Constructional score on the RBANS, another measure that assesses for visuospatial ability. Perceptual reasoning is one of the domains cited as important to assess by the NINDS and the PRI is a recommended measure to assess this domain of functioning (NINDS CDE Team, 2010).

Language. Language was assessed using a composite score consisting of average scores from the Similarities subtest of the WAIS-IV and Boston Naming Test.

The Similarities subtest is one of the subtests of the WAIS-IV that assesses for language ability. The individual is asked to compare two words and verbalize the ways in which they are similar. The Similarities subtest has a reported high reliability score (α= .87) and a moderate convergent validity of r =.52 with the RBANS Language score. Language is an important area of study in epilepsy and scores on the Similarities subtest has been previously used in the literature to assess for language functioning in epileptic populations (NINDS CDE Team, 2010; Milberg, Greiffenstein, Lewis, & Rourke, 1980).

The Boston Naming Test (BNT) was used as part of the composite to assess for language ability. Individuals were presented with pictures and given a time limit to identify the picture before cues were given (Strauss et al., 2006). The BNT demonstrates moderate to high reliability scores (.76 to .91) and moderate convergent validity with other naming measures such as the naming subtest of the NAB (r = .50; Yochim, Kane, & Mueller, 2009; Strauss et al., 2006; Flanagan & Jackson, 1997). Language is an essential assessment in epilepsy and the BNT is one of the most widely used measures to assess for

language functioning in epileptic populations (Janecek et al., 2013; Marino et al., 2009; Prigatano & Kirlin, 2009; Fargo et al., 2004)

Executive functioning. Executive functioning was assessed using a composite score consisting of an average score from the Trail Making Test B (TMTB) and the Ruff Figural Fluency Test (RFFT).

Trail Making Test B requires individuals to connect alternating numbers and letters in alternating alpha-numeric order (Strauss et al., 2006). Studies have reported a reliability score of .70 for the TMTB (Strauss et al., 2006). TMTB has also demonstrated moderate validity with executive functioning measures such as Digit Backward ($r = -.54$; Sánchez-Cubillo et al., 2009). Set shifting is an important aspect of executive functioning to assess for in epileptic populations (NINDS CDE Team, 2010). TMTB is commonly used in the literature to assess for this domain in adults and children with epilepsy (Hudson, Flowers, & Walster, 2014; Longo, Kerr, & Smith, 2013; Liik et al., 2009; Locke et al., 2006)

The Ruff Figural Fluency Test (RFFT) was used to assess for executive functioning, specifically cognitive flexibility. The individual is presented with different patterns of stimulus dots and then asked to draw as many figures as possible given the different dot configurations. (Jones-Gotman & Milner, 1977). RFFT demonstrated acceptable to high reliability scores for the total number of unique designs (.71-.88) and small to moderate convergent validity with other measures of executive functioning such as the Wisconsin Card Sorting Test Perseverative Responses (Ross, 2014; Basso et al., 1999; Demakis & Harrison, 1997). Executive functioning, as noted above, is an important

area to assess in epilepsy and the RFFT is awidely-used tests to assess for nonverbal fluency (Strauss et al., 2006).

Subjective Cognitive Measures

Neuro-QOL: Applied Cognition—General Concerns. The Applied Cognitions – General Concerns subscale is an 8-item self-report measure of perception of overall cognitive ability (NINDS, 2012). Respondents indicate their experiences in the past 7 days using a Likert scale ranging from 1, not at all, to 5, very much, indicating the difficulty with which they experience with each item (NINDS, 2012). The measure demonstrates good reliability (alpha coefficient = .94) and it has demonstrated a moderate to high convergent validity (r = .784) with the cognitive subscale of the QOLIE-31 (Victorson et al., 2014; Nowinski et al., 2012). A full list of questions in this measure can be found in Appendix A.

Neuro-QOL: Applied Cognition – Executive Functioning. The Applied Cognitions—Executive Functioning subscale is an 8-item self-report measure of subjective executive functioning within the past week (NINDS, 2012). Respondents indicate the frequency with which they have had difficulty with each item using a Likert scale ranging from 1, never, to 5, very often (several times a day). The alpha coefficient of the measure is .94 and it has moderate to high convergent validity (r = .668) with the cognitive subscale of the QOLIE-31 (Victorson et al., 2014; Nowinski et al., 2012). A full list of questions in this measure can be found in Appendix B.

Psychiatric Symptomology

Self-reported psychiatric symptomology of depression and anxiety were assessed using T scores from the Personality Assessment Inventory Anxiety (ANX) and Depression (DEP) scales. The PAI is a 344-item self-report measure that assesses various aspects of personality and mood (Strauss et al., 2006; Morey, 1991). Responses follow a Likert scale format on a 4-point scale (false, slightly true, true, mainly true and very true). Both the Anxiety and Depression clinical scales have demonstrated high reliability scores (.90 for ANX and .87 for DEP; Morey, 1991). Additionally, both the Anxiety and Depression scales have well-established convergent validity with other measures of anxiety and depression, respectively. The Anxiety scale has correlations of .62 to the Beck Anxiety Inventory while the Depression scale has a reported correlation of .80 with the Beck Depression Inventory (Morey, 1991). As depression and anxiety symptomology is common in epileptic populations and impactful on quality of life, their assessment is essential. The PAI is a commonly used measure in the epileptic literature to assess these domains (Locke et al., 2011; Testa et al., 2011; Gale & Hill, 2012; Thompson et al., 2010).

Data Analysis

Statistical analysis consisted of Spearman's rho correlations between the subjective cognitive measures (Neuro QOL: Applied Cognitions—General Concerns and Neuro QOL: Applied Cognitions Executive Functioning) and objective cognitive measures (composite scores in visual skills, language, memory, executive functioning, processing speed, and attention/working memory). Additionally, linear regressions were calculated in order to address whether depression and anxiety would emerge as significant predictors of subjective cognitive functioning on the NeuroQOL, over and

above the predictive ability of objective cognitive variables. Lastly, specificity and sensitivity calculations were conducted in conjunction with ROC curves in order to explore the specificity and sensitivity of subjective cognitive complaints for objective cognitive impairment.

To account for multiple analyses, the false discovery rate (FDR) was used. The FDR offers an increase in power of the analyses while still maintaining boundaries on error rates. The FDR controls for the expected proportion of errors among rejected hypotheses rather than familywise error rates, which traditional Bonferroni procedures control for, and is therefore a less stringent control of Type I error (Benjamini & Hochberg, 1995). As this study is exploratory in nature with a small sample size, the FDR allows for the discovery of more significant relationships while still reasonably controlling for the error rate of performing multiple analyses. To calculate the FDR, the overall acceptable rate of false discovery rate was set to 5%. The ordered *p* values of all analyses were evaluated against the ratio of the rank ordered analysis to the total number of analyses conducted, multiplied by the acceptable false discovery rate. The corrected significance value yielded a q^* value of .02; *p* values in excess of this value were discarded as potentially false discoveries. As the fourth aim is exploratory in nature, the FDR was not used.

CHAPTER THREE

Results

Demographics

Forty-six charts from the Scott and White epilepsy clinic were reviewed, and thirty-nine were included in the current study. Five cases were removed from data analysis due to incomplete score profiles for the cognitive composite scores. An additional two were removed due to a raw score of less than 45 on the TOMM 2, which is suggestive of insufficient effort on the objective cognitive testing to yield valid data. The average age of the sample was 41.9 years old (SD=2.5). The average years of education of the sample was 12.7 years (SD= 3.9 years). There were 24 females (62%) and 15 males (38%). Twenty of the cases were diagnosed with epilepsy alone (51%), 10 with psychogenic non-epileptic events (26%), and 9 with a mixture of both epilepsy and psychogenic events (23%).

Patients were assessed with a variety of cognitive and neuropsychological measures. Composite cognitive measures were created by taking the average of two subtests scores within each domain. The perceptual reasoning composite score is comprised of the average of the demographically-adjusted WAIS-IV Matrix Reasoning and WAIS-IV Block Design scores. The processing speed composite score consists of the average of the WAIS-IV Digit-Symbol Coding and WAIS-IV Symbol Search scores. The working memory composite score is the average of the WAIS-IV Arithmetic and WAIS-IV Digit Span scores. The memory composite score is an average of the WMS-IV Visual Reproduction Delayed II score and the California Verbal Learning Test-2 Delayed Recall

score. The executive functioning composite consists of the average of the Figural Fluency score and Trail Making Test B score. Finally, the language composite score is the average of the WAIS-IV Similarities score and Boston Naming Test score. Descriptive statistics for the individual subtest scores and composite scores are presented in Table 1. The scores from the patients' subjective measures of cognition (ACGC and ACEF) as well as their emotional functioning scores are shown in Table 2. Descriptive statistics for the patients' cognitive domains, emotional functioning, and subjective cognitive functioning for each diagnostic category are presented in Table 3. A Kruskal-Wallis H test was performed to assess for differences in these domains of functioning across the diagnostic categories of epilepsy, PNEE, and PNEE with comorbid epilepsy. Results indicated that there was a statistically significant difference in the memory composite measure between the diagnostic categories, $\chi^2(2) = 7.009$, $p = .03$, with a mean rank memory score of 22.2 for the epilepsy group, 15.0 for the PNEE group, and 20.6 for the PNEE with comorbid epilepsy group. Post-hoc analysis demonstrated that composite memory T-scores for the epilepsy group were significantly higher than both the PNEE and PNEE with comorbid epilepsy groups. There was no difference between the PNEE and PNEE with comorbid epilepsy group. Lastly, Spearman's rho was used to provide descriptive correlation analyses on the sample as a whole. The results are presented in Table 4.

The first aim sought to explore the relationship between the subjective and objective measures of cognition. The results did not support the hypothesis that there would be small to moderate correlations between the objective cognitive composite scores and subjective cognitive complaint measures. As an initial step prior to data analysis, each variable was tested for assumptions for normality and homogeneity of

variance. The histograms, skewness, kurtosis statistic, and the Shapiro-Wil's test all strongly suggest that not all of the data are normally distributed. Descriptive and normality statistics for the variables used in the analysis are presented in Table 1, 2, 3, and 4. As a result of the violations of normality, Spearman's rho was used to assess for correlation between the subjective cognitive measures and objective cognitive measures. Correlations were conducted between each of the six composite T-scores (memory, processing speed, attention/working memory, visual skills, language, and executive functioning) and the Neuro-QOL: Applied Cognition Measures (e.g. general concerns and executive functioning) for the sample as a whole. The results appear in Table 5.

Results from the correlation matrix indicated no significant correlations between any of the objective measured domains of cognition (e.g. PRI, PSI, EF, Mem, WM, Lang) and either of the subjective measures of cognition (e.g. ACGC, ACEF) for the sample as a whole.

The second aim sought to explore the specificity and sensitivity of subjective cognitive complaints to objective cognitive impairment. The results support the hypothesis that subjective cognitive measures would have high sensitivity but low specificity to objective cognitive impairments. ROC curves and sensitivity and specificity rates were calculated for each of the subjective measures (e.g. ACGC and ACEF) for each of the cognitive domains (PRI, PSI, EF, WM, Mem, Lang). For the purposes of this study, objective cognitive impairment is defined as having a T-score below 40 on any of the composite scores (PRI, PSI, EF, Mem, WM, Lang). Subjective cognitive impairment is defined as having a T-score below 40 on either the ACGC or ACEF, as lower scores

are associated with greater perceived cognitive dysfunction. The rates of cognitive impairment for all six cognitive domains by this definition are listed in Table 6.

Table 1

Objective Cognitive Functioning T-scores

Cognitive Measure	N	Mean	Standard Deviation
Average PRI	**39**	**39.60**	**15.39**
WAIS-IV MR	39	41.64	17.05
WAIS-IV BD	39	37.56	16.31
Average PSI	**39**	**35.72**	**15.68**
WAIS-IV DSC	39	35.48	15.00
WAIS-IV SyS	39	35.94	18.02
Average WM	**39**	**38.12**	**13.21**
WAIS-IV Arith	39	35.44	17.88
WAIS-IV DS	39	40.79	13.14
Average Lang	**39**	**37.04**	**15.45**
WAIS-IV Sim	39	37.43	17.52
BNT	39	36.64	15.41
Average EF	**39**	**31.11**	**13.47**
TMT B	39	38.46	16.35
FigFlu	38	24.39	18.20
Average Mem	**39**	**39.31**	**13.23**
WMS-IV VR II	39	37.59	19.36
CVLT2 – DR	39	41.03	13.24

Note. PRI represents visual skills composite score, WAIS-IV MR represents Wechsler Adult Intelligence Scale – Fourth Edition Matrix Reasoning, WAIS-IV BD represents Wechsler Adult Intelligence Scale – Fourth Edition Block Design, PSI represents processing speed composite score, WAIS-IV DSC represents Wechsler Adult Intelligence Scale – Fourth Edition Digit Symbol Coding, WAIS-IV SyS represents Wechsler Adult Intelligence Scale – Fourth Edition Symbol Search, WM represents attention/working memory composite score, WAIS-IV Arith represents Wechsler Adult Intelligence Scale – Fourth Edition Arithmatic, WAIS-IV DS represents Wechsler Adult Intelligence Scale – Fourth Edition Digit Span, Lang represents language composite score, WAIS-IV Sim represents Wechsler Adult Intelligence Scale – Fourth Edition Similarities, BNT represents Boston Naming Test, EF represents executive functioning composite score, TMT B represents Trail-Making Test B, FigFlu represents Figure Fluency, Mem represents memory composite score, WMS-IV VR II represents Wechsler Memory Scales – Fourth Edition Visual Reproduction Delayed II, CVLT-2 DR represents California Verbal Learning Test – 2nd Edition Delayed Recall

Table 2

Emotional and Subjective Cognitive Functioning T-scores

Measure	N	Mean	Standard Deviation
ACGC	39	33.28	8.85
ACEF	39	34.01	10.70
PAI DEP	39	63.51	19.70
PAI ANX	39	60.69	18.46

Note. ACGC represents NeuroQoL Applied Cognitions—General Concerns, ACEF represents NeuroQoL Applied Cognitions—Executive Functioning. PAI DEP represents Personality Inventory Assessment Depression Scale, PAI ANX represents Personality Inventory Assessment Anxiety Scale, Higher T-scores on the PAI DEP and PAI ANX represent increased symptoms. Lower T-scores on the ACGC and ACEF represent worse perceived cognitive functioning.

Table 3

Objective Cognitive, Emotional, and Subjective Cognitive Functioning T-scores for Patients Diagnosed with Epilepsy, PNEE, and PNEE with Comorbid Epilepsy

Variable	Epilepsy = 20			PNEE = 10			PNEE + Epilepsy = 9			Sig. Diff
	Mean	SD	Med	Mean	SD	Med	Mean	SD	Med	
ACGC	35.41	9.75	34.80	32.14	6.02	32.20	29.79	8.86	27.80	N
ACEF	33.01	10.48	32.55	32.15	7.88	31.70	38.29	13.60	36.90	N
PAI DEP	66.20	12.87	68.00	56.10	33.88	63.00	65.78	8.12	65.00	N
PAI ANX	61.45	11.96	59.00	54.70	31.43	60.00	65.67	9.63	63.00	N
PRI	43.33	14.41	45.75	30.90	19.67	38.75	41.00	8.06	39.00	N
PSI	40.43	15.27	43.25	28.85	16.50	29.25	32.89	13.58	36.00	N
EF	33.08	15.45	37.88	25.48	12.81	23.00	32.98	7.52	34.85	N
MEM	44.63	11.64	47.00	33.10	15.40	36.25	34.39	9.81	35.00	Y
WM	40.28	12.05	41.75	32.80	15.23	34.00	39.22	13.22	39.50	N
LANG	41.63	11.72	44.25	31.70	18.94	35.75	32.79	17.19	32.50	N

Note. ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score, PAI DEP represents Personality Inventory Assessment Depression Scale, PAI ANX represents Personality Inventory Assessment Anxiety Scale, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score, NS represents not significant, MIXED represents PNEE with comorbid epilepsy.

Table 4

Spearman Correlations Between Objective Cognitive, Emotional, and Subjective Cognitive Measures for the Sample as a Whole

Meas	ACGC	ACEF	DEP	ANX	PRI	PSI	EF	MEM	WM	LANG
ACGC	-	-	-	-	-	-	-	-	-	-
ACEF	-.886**	-	-	-	-	-	-	-	-	-
DEP	-.451**	.338*	-	-	-	-	-	-	-	-
ANX	-.322*	.196	.721**	-	-	-	-	-	-	-
PRI	-.048	.026	.196	-.143	-	-	-	-	-	-
PSI	-.160	.205	.065	-.108	.537**	-	-	-	-	-
EF	.051	-.061	.311	.298	.579**	.553**	-	-	-	-
MEM	-.046	.047	.105	-.040	.533**	.545**	.365*	-	-	-
WM	-.058	.061	.221	.101	.691**	.678**	.644**	.641**	-	-
LANG	-.014	.064	-.095	-.183	.613**	.575**	.353*	.645**	.673**	-

Note. ** Denotes significance at the .01 level. * Denotes correlation is significant at the .05 level. Meas represents Measures, PNEE represents psychogenic non-epileptic events, ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score, DEP represents Personality Inventory Assessment Depression Scale, ANX represents Personality Inventory Assessment Anxiety Scale, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score.

Table 5

Correlations Between Composite Cognitive Scores and Neuro QoL Scales

Measure	PRI	PSI	EF	Mem	WM	Lang
ACGC	-.048	-.160	.051	-.046	-.058	-.014
ACEF	.026	.205	-.061	.047	.061	.064

Note. PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score, ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score

Sensitivity is defined in this study as the proportion of patients who have cognitive impairment, as defined by a T-score of less than 40 on PRI, PSI, EF, Mem, WM or Lang, and who also report subjective cognitive impairment, as defined by a T-score of less than 40 on either the ACGC or ACEF. Analyses of the ROC curves did not yield a more optimal cutoff point. Area under the curve for the ROC plots for each cognitive domain were between 0.5 and 0.6, which are similar to proportions expected from random chance. Therefore, the 40 T-score cutoff scores were used instead for the sensitivity and specificity calculations. Sensitivity assesses for the probability that subjective measures of cognition identify the presence of objective cognitive impairment. Sensitivity is calculated by dividing the number of patients with cognitive impairment who report subjective cognitive impairment by the total number of patients with objective cognitive impairment.

Specificity is defined as the proportion of people who do not have cognitive impairment who do not report subjective cognitive impairment. In other words, the probability of subjective measures of cognition to identify lack of objective cognitive impairment. Specificity is calculated by dividing the number of patients without cognitive impairment and who do not report subjective cognitive impairment by the total number of patients without cognitive impairment.

The results indicate that both subjective measures of cognition (Neuro QOL: Applied Cognitions – General Concerns and Neuro QOL: Applied Cognitions – Executive Functioning) demonstrate high sensitivity for impairments in all six domains of cognition (visual skills, processing speed, executive functioning, memory,

attention/working memory, language) but also low specificity for all six domains. The results appear in Table 7.

Table 6

Rates of Impairment in Cognitive Domains

Measure	N (out of 39)	%
PRI	19	48.72
PSI	24	61.54
EF	28	71.79
MEM	17	43.59
WM	21	53.85
LANG	18	46.15

Note. PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score

Table 7

Sensitivity and Specificity of the Neuro QoL: Applied Cognitions – General Concerns and Neuro QoL: Applied Cognitions – Executive Functioning Measures with Cut-off Point of T < 40 Defining Cognitive Impairment

Measures	Sensitivity (%)	Specificity (%)
AGCG for PRI	84.21	20.00
AGCG for PSI	83.33	13.33
AGCG for EF	82.14	18.18
AGCG for Mem	82.35	18.18
AGCG for WM	80.95	16.67
AGCG for Lang	77.78	19.05
ACEF for PRI	73.68	25.00
ACEF for PSI	75.00	33.33
ACEF for EF	71.43	18.18
ACEF for Mem	82.35	36.36
ACEF for WM	71.43	27.78
ACEF for Lang	77.78	28.57

Note. ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score

The third aim was to explore depression and anxiety as predictors of subjective cognitive functioning on the ACGC and ACEF. The results partially support the

hypothesis for this aim in that depression but not anxiety emerged as a significant predictor of one of the measures of subjective cognitive complaints on the NeuroQOL. With regard to the assumptions, each predictor was plotted against each measure of subjective cognitive functioning and visually assessed for the assumption of linearity. No curvilinear relationships emerged for any of the predictors tested. The assumption of normality of the residuals was addressed by graphing the residuals following the linear regressions and running descriptive statistics on them. The assumption of homoscedasticity, or error variance, was addressed through plots of the residuals versus the subjective measures of cognition. Lastly, collinearity was assessed using the regression analysis provided by SPSS. The results yielded one significant regression equation ($F(1,37) = 7.043$, $p < .02$), with an R^2 of .16. Depression, as measured by the T-score on the PAI, significantly predicted the Neuro QoL: Applied Cognitions – General Concerns score ($\beta = -.40$, $p < .02$). Depression also predicted and the Neuro QoL: Applied Cognitions – Executive Functioning score ($F(1,37) = 4.467$, $p < .05$, with an R^2 of 0.108). However, this is not considered significant due to the calculated q-value of the FDR. No other statistically significant predictors emerged for either measures of subjective cognitive functioning on the ACGC or ACEF.

The secondary aim of this study was to explore potential differences between diagnostic groups (i.e. PNEE, epilepsy or PNEE with comorbid epilepsy) in terms of the relationships between subjective cognitive complaints and objective cognitive deficits. The results support the initial study hypothesis that there would be minimal differences in the relationship between subjective cognitive complaints and objective cognitive deficits between epilepsy, PNEE, and PNEE with comorbid epilepsy groups. In order to address

this, correlations were conducted between the subjective and objective measures of cognition. Spearman's rho was used to assess for correlation between the subjective cognitive measures and objective cognitive measures within each diagnostic category. Results are presented in Table 8, 9, and 10.

Results found no significant correlations between any of the objective domains of cognition (e.g. PRI, PSI, EF, Mem, WM, Lang) and either of the subjective measures of cognition (e.g. ACGC, ACEF) in any of the diagnostic categories. However, the extremely small sample sizes mean that the it would be unlikely for these correlations to reach statistical significance. These results failed to find any significant difference between diagnostic groups in terms of the relationships between subjective cognitive complaints and objective cognitive deficits.

Table 8

Correlations Between Composite Scales and Neuro QoL Scales in Patients Diagnosed with Epilepsy

Measures	PRI	PSI	EF	Mem	WM	Lang
ACGC	-.018	-.184	.170	-.027	.110	.119
ACEF	.076	.171	-.174	.035	-.081	.047

Note. PNEE represents psychogenic non-epileptic events, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score, ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score.

Table 9

Correlations Between Composite Scales and Neuro QoL Scales in Patients Diagnosed with PNEE

Measures	PRI	PSI	EF	Mem	WM	Lang
ACGC	-.512	-.268	-.335	-.474	-.529	-.104
ACEF	.134	.286	.103	.188	.370	-.267

Note. PNEE represents psychogenic non-epileptic events, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score, ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score

Table 10

Correlations Between Composite Scales and Neuro QoL Scales in Patients Diagnosed with PNEE with Comorbid Epilepsy

Measures	PRI	PSI	EF	Mem	WM	Lang
ACGC	-.137	-.225	.253	-.277	.025	-.504
ACEF	.077	.475	-.253	.366	.059	.607

Note. PNEE represents psychogenic non-epileptic events, PRI represents visual skills composite score, PSI represents processing speed composite score, EF represents executive functioning composite score, Mem represents memory composite score, WM represents attention/working memory composite score, Lang represents language composite score, ACGC represents Neuro QoL: Applied Cognition – General Concerns score, ACEF represents Neuro QoL: Applied Cognition – Executive Functioning score

CHAPTER FOUR

Discussion

The purpose of study was to explore the relationship between subjective cognitive complaints and objective cognitive deficits in patients with epilepsy, psychogenic non-epileptic events (PNEE), or PNEE with comorbid epilepsy, explore the specificity and sensitivity of subjective cognitive measures in comparison to objective cognitive measures, and explore depression and anxiety as predictors of subjective cognitive functioning. A secondary aim was to explore the differences between PNEE, epileptic, and PNEE with comorbid epilepsy groups in terms of the relationship between subjective cognitive complaints and objective cognitive deficits.

With regard to the first aim, results did not indicate a statistically significant relationship between the objective measures of cognition (visual skills, processing speed, executive functioning, memory, attention/working memory and language) and the subjective measures of cognition. These results are in contrast with the hypothesis for this aim which stated that there would be a small to moderate relationship between the objective cognitive deficits and subjective cognitive complaints. These results are not entirely unexpected as prior studies in the epilepsy literature found no significant relationship between subjective and objective measures (Galioto, Blum, & Tremont, 2015; Liik, et al., 2009; Baxendale & Thompson, 2005; Baños et al., 2004; Fargo et al., 2004; Jungwirth et al., 2004; Piazzini, et al., 2001). Additionally, among studies with results that have demonstrated significant relationships between objective and subjective

measures of cognition, there is a lack of agreement on the direction of the relationship, with some studies finding that there is an overestimation of cognitive abilities while some studies finding an underestimation (Fargo et al., 2004; Piazzini et al., 2001). While there are fewer studies looking at the relationship between subjective and objective measures of cognition in patients with psychogenic non-epileptic events, there is a similar lack of agreement in the literature regarding this relationship in the PNEE population (Prigatano & Kirlin, 2009; Fargo et al., 2004). Clinically, these results suggest that in this population, patients' report of cognitive complaints are not reliable means to assess for the presence or absence of objective cognitive deficits as no clear relationship exists between them in this study. As a result, objective cognitive assessments should be used in individuals with cognitive complaints to determine whether there is cognitive deficit and clarify the domains of cognitive deficit.

With respect to the specificity and sensitivity of the Neuro QoL: Applied Cognitions – General Concerns and Neuro QoL: Applied Cognitions – Executive Functioning, both measures demonstrated high sensitivity and low specificity for impairments in all six domains assessed (visual skills, processing speed, executive functioning, memory, attention/working memory and language). These results support the hypothesis that subjective cognitive measures are sensitive to cognitive impairment but have low specificity to cognitive impairments. In other words, a majority of patients with objective cognitive deficits, as measured by objective measures of cognition, also report subjective cognitive complaints, as measured by subjective measures of cognition. Notably, the Neuro QoL: Applied Cognitions – General Concerns measure appears to be particularly sensitive (78-84%) to deficits across cognitive domains. While high

sensitivity is encouraging, the majority of respondents report cognitive complaints regardless of the presence of cognitive impairments, resulting in extremely low specificity. These results are consistent with numerous studies in the literature that report patients with epilepsy, PNEE, and PNEE with comorbid epilepsy indicate high levels of subjective cognitive complaints (Myers et al., 2012; Rayner et al., 2010; Prigatano & Kirlin, 2009; Baños et al., 2004; Fargo et al., 2004; Szaflarski et al., 2003; Elixhauser et al., 1999; Breier et al., 1998; Giovagnoli et al., 1997). While not unexpected, the low specificity of the Neuro QoL: Applied Cognition measures detract from its diagnostic value in a clinical setting because reports of subjective cognitive complaints do not always reflect objective cognitive deficits. These results further highlight the necessity of objective cognitive measures when working with this population and the need for better diagnostic tools that could shed light on a patient's objective cognitive functioning using his or her subjective cognitive complaints. Currently, there are very few studies in the literature that examine the sensitivity or specificity of subjective measures of cognition in these populations. The current study highlights this issue for providers in the field.

In terms of significant predictors for subjective cognitive complaints, the T-score on the depression scale of the PAI emerged as the only significant predictor of subjective cognitive complaints, namely the Neuro QoL: Applied Cognitions – General Concerns, but not the Neuro QoL: Applied Cognitions – Executive Functioning measure. These results partially support the hypothesis that both anxiety and depression scales on the PAI would emerge as significant predictors for subjective cognitive functioning. In this study, the anxiety measure did not appear to be a significant predictor of either measure of subjective cognitive functioning. While the depression scale on the PAI significantly

predicted only one of the subjective cognitive measures of cognition, it should be noted that the lack of significance for the Neuro QoL Applied Cognitions – Executive Functioning scale is most likely due to the small sample size of the study. The adjusted significance level of the FDR, which is based on the number of analyses performed in this study, precluded the finding that depression is a significant predictor of the Neuro QoL Applied Cognitions – Executive Functioning scale. However, there is strong evidence in the literature demonstrating that emotional disturbances such depression are predictive for subjective cognitive complaints in patients with epilepsy and PNEE (Souza, Fonseca, Augusto, & Trindade, 2016; Brown et al., 2014; Galioto et al., 2013; Giovagnoli, 2013; Rösche et al., 2012; Rayner et al., 2010; Liik et al., 2009; Marino et al., 2009; Lahr et al., 2007; Au et al., 2006; Baños et al., 2004; Piazzini et al., 2001; Elixhauser et al., 1999). In particular, numerous studies have found depression to be a significant predictor for subjective memory complaints (Galioto et al., 2015; Rayner et al., 2010; Salas-Puig et al., 2009). Additionally, subjective cognitive complaints are part of the depression symptomology. One of the criteria used to diagnose Major Depressive Disorder in the DSM-5 include "poor concentration" (DSM-5). Common self-report measures for depression such as the Beck Depression Inventory also include subjective cognitive complaints related to decision making (Beck, Steer, & Brown, 1996). Clinically, these results strongly suggest that patients who report subjective cognitive complaints likely experience symptoms of depression. Therefore, treatment plans with interventions that target symptoms for depression should also mitigate patients' subjective cognitive complaints. There are fewer studies to address the role that anxiety plays in cognitive complaints in epilepsy and PNEE populations. The few that do report results similar to

those for depression in that it is predictive of subjective cognitive complaints (Salas-Puig et al., 2009; Piazzini et al., 2001), which is not consistent with the results of this study. This may be attributed to the study's limitation of a small sample size, but may require further exploration of the difference in relationship between depression and anxiety with subjective cognitive functioning.

Lastly, regarding the secondary aims of the study, the results did not yield any significant relationships between the objective measures of cognition and subjective measures of cognition in any of the diagnostic categories, though sample sizes were extremely small for each group. While some of the relationships may have been significant in the PNEE group if the magnitude held in a larger sample, the relationships are inconsistent in between the diagnostic categories. For example, there were negative correlations between objective measures (i.e. better performance objectively, more cognitive complaints) for general cognition and PRI scores, but the opposite pattern for executive functioning. A similar pattern was observed for processing speed and working memory. Therefore, if there is a relationship between objective and subjective cognitive functioning across diagnostic categories, it does not appear to have a consistent pattern.

Still, it remains possible that there are significant differences in the relationships between subjective and objective measures of cognition between these diagnostic categories that this sample could not detect. For example, patients who have epilepsy may have greater and more robust relationships between subjective and objective measures of cognition as compared to patients who have been diagnosed with solely PNEE or PNEE with comorbid epilepsy. Additionally, because the magnitude and type of psychological disturbance may be variable between epilepsy, PNEE, and combined

groups, the impact of psychopathology on cognitive status and in turn, cognitive complaints may be variable. In short, there remain unanswered questions about how subjective and objective cognitive complaints may be derived within these individual subsamples.

Implications

Overall, these results have several clinical implications, the most prominent and arguably important of which is that patients' report of cognitive difficulties likely do not reflect objective cognitive deficits. Results from the correlation and regression analyses demonstrate that subjective cognitive complaints as measured by the NeuroQOL: Applied Cognition measures are not reliable indicators for objective cognitive impairment. Rather, patients' subjective cognitive complaints likely reflect their emotional state, more specifically, symptoms related to depression. Therefore, in epilepsy clinic settings, objective cognitive measures should be given patients who report cognitive complaints whenever possible so that clinicians can determine whether there is any area of cognitive deficit and clarity the domains of deficit if they exist. As one of the benefits of using the Neuro-QOL is that it provides a standardized way to measure various symptoms of interest across various conditions, it would be interesting to see whether the results of this study would hold true in larger, epidemiological studies for epilepsy as well as for other disorders whose symptoms include subjective cognitive complaints and objective cognitive deficits.

Limitations

This study has several limitations. The first limitation is its sample size. Many patients were excluded due to incomplete test data and some for poor effort. Due to the retrospective nature of the study, it was not possible to follow up with these patients to address some of these issues. The small sample not only affected the significance levels for the analyses in the study, it is possible that the findings would be less generalizable to populations at other epilepsy clinics. Additionally, within the epilepsy group, the patients had heterogeneous epilepsy diagnosis. Some were diagnosed with generalized epilepsy while others were diagnosed with partial epilepsy. Future studies that utilize a more homogeneous epileptic population may yield different results. Lastly, a sizeable proportion of the population used in this study were diagnosed with PNEE with comorbid epilepsy. While this is an important population to study and better understand, the inclusion of this population often complicates data analysis and makes data difficult to interpret, particularly when ascertaining for differences across diagnostic categories.

Future Studies

Future studies should be conducted to further clarify the relationship between objective and subjective measures of cognition within the epilepsy and PNEE populations in general. More specifically, these results raise the question of whether relationships between subjective and objective measures of cognition are similar across the different diagnostic categories (e.g. epilepsy, PNEE, and PNEE with comorbid epilepsy). Along the same lines, future studies could contrast the number and severity of psychological symptoms between epileptic and PNEE populations and explore the relationship that those symptoms may have with subjective and objective cognitive function. There is also

a need for studies that examine the sensitivity and specificity of subjective measures of cognition in epileptic and PNEE populations, particularly given the lack of correlation between subjective and objective measures of cognition found in this study. Lastly, future studies should explore the role that anxiety may play in cognitive complaints in epileptic and PNEE populations. Additional research is needed to fully determine the relationship between anxiety and subjective cognitive complaints and the relationship between depression and cognitive complaints.

Conclusions

This study did not find a significant relationship between subjective and objective measures of cognition among patients with epilepsy, PNEE, or PNEE with comorbid epilepsy. The subjective measures of cognition used in this study demonstrated high sensitivity and low specificity for cognitive impairments in visual skills, processing speed, executive functioning, memory, attention/working memory, and language. Depression was a significant predictor of subjective measures of cognition. Exploratory analysis failed to find any significant differences in the relationship between subjective and objective measures of cognition between diagnostic criteria (i.e. epilepsy, PNEE, or PNEE with comorbid epilepsy). Future studies are needed to further clarify and understand the relationship or lack of relationship between subjective cognitive complaints and objective cognitive deficits in these populations.

APPENDICES

APPENDIX A

Table A.1.

Neuro QoL: Applied Cognition – General Concerns

In the past 7 days…	Not at all	A little bit	Somewhat	Quite a bit	Very much
My mind has been as sharp as usual…					
My memory has been as good as usual…					
My thinking has been as fast as usual…					
I have been able to keep track of what I am doing, even if I am interrupted…					
I have been able to concentrate…					
I have been able to think clearly without extra effort…					
I have been able to pay attention and keep track of what I am doing without extra effort…					
I have been able to remember things as easily as usual without extra effort…					

APPENDIX B

Table B.2.

Neuro QoL: Applied Cognition – Executive Functioning

In the past 7 days…	Never	Rarely (Once)	Sometimes (Two or three times)	Often (About once a day)	Very often (Several times a day)
My thinking has been slow…					
It has seemed like my brain was not working as well as usual…					
I have had to work harder than usual to keep track of what I was doing…					
I have had trouble shifting back and forth between different activities that require thinking…					
I have had trouble concentrating…					
I have had to work really hard to pay attention or I would make a mistake…					
I have had trouble forming thoughts…					
My problems with memory, concentration, or making mental mistakes have interfered with the quality of my life…					

REFERENCES

Ahmedani, B. K., Osborne, J., Nerenz, D. R., Haque, S., Pietrantoni, L., Mahone, D., & Smith, B. J. (2013). Diagnosis, costs, and utilization for psychogenic non-epileptic seizures in a US health care setting. *Psychosomatics*, *54*(1), 28–34.

Asadi-Pooya, A. A., & Sperling, M. R. (2015). Epidemiology of psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *46*, 60-65.Au, A., Leung, P., Kwok, A., Li, P., Lui, C., & Chan, J. (2006). Subjective memory and mood of Hong Kong Chinese adults with epilepsy. *Epilepsy & Behavior*, *9*(1), 68–72. http://doi.org/10.1016/j.yebeh.2006.04.004

Aydemir, N., Özkara, Ç., Ünsal, P., & Canbeyli, R. (2011). A comparative study of health related quality of life, psychological well-being, impact of illness and stigma in epilepsy and migraine. *Seizure*, *20*(9), 679

Baños, J. H., LaGory, J., Sawrie, S., Faught, E., Knowlton, R., Prasad, A., … Martin, R. C. (2004). Self-report of cognitive abilities in temporal lobe epilepsy: cognitive, psychosocial, and emotional factors. *Epilepsy & Behavior*, *5*(4), 575–579. http://doi.org/10.1016/j.yebeh.2004.04.010

Barr, W. B. (2007). Epilepsy and Neuropsychology: Past, Present, and Future. *Neuropsychology Review*, *17*(4), 381–383. http://doi.org/10.1007/s11065-007-9045-7

Baslet, G. (2011). Psychogenic non-epileptic seizures: A model of their pathogenic mechanism. *Seizure*, *20*(1), 1–13. http://doi.org/10.1016/j.seizure.2010.10.032

Baxendale, S., & Thompson, P. (2005). Defining meaningful postoperative change in epilepsy surgery patients: Measuring the unmeasurable? *Epilepsy & Behavior*, *6*(2), 207–211. http://doi.org/10.1016/j.yebeh.2004.12.009

Begley, C. E., Famulari, M., Annegers, J. F., Lairson, D. R., Reynolds, T. F., Coan, S., ... & Rocca, W. A. (2000). The cost of epilepsy in the United States: an estimate from population-based clinical and survey data. *Epilepsia*, *41*(3), 342-351.

Benbadis, S. R., Agrawal, V., & Tatum, W. O. (2001). How many patients with psychogenic nonepileptic seizures also have epilepsy? *Neurology*, *57*(5), 915–917.

Benbadis, S. R., & Allen Hauser, W. (2000). An estimate of the prevalence of psychogenic non-epileptic seizures. *Seizure*, *9*(4), 280–281. http://doi.org/10.1053/seiz.2000.0409

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the royal statistical society. Series B (Methodological)*, 289-300.

Bettini, L., Croquelois, A., Maeder-Ingvar, M., & Rossetti, A. O. (2014). Diagnostic yield of short-term video-EEG monitoring for epilepsy and PNESs: A European assessment. *Epilepsy & Behavior*, *39*, 55–58. http://doi.org/10.1016/j.yebeh.2014.08.009

Binder, L. M., Salinsky, M. C., & Smith, S. P. (1994). Psychological correlates of psychogenic seizures. *Journal of Clinical and Experimental Neuropsychology*, *16*(4), 524-530.

Bodde, N. M. G., Brooks, J. L., Baker, G. A., Boon, P. A. J. M., Hendriksen, J. G. M., Mulder, O. G., & Aldenkamp, A. P. (2009). Psychogenic non-epileptic seizures—Definition, etiology, treatment and prognostic issues: A critical review. *Seizure*, *18*(8), 543–553. http://doi.org/10.1016/j.seizure.2009.06.006

Breier, J. I., Fuchs, K. L., Brookshire, B. L., Wheless, J., Thomas, A. B., Constantinou, J., & Willmore, L. J. (1998). Quality of life perception in patients with intractable epilepsy or pseudoseizures. *Archives of neurology*, *55*(5), 660-665.Brown, R. J., Syed, T. U., Benbadis, S., LaFrance, W. C., & Reuber, M. (2011). Psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *22*(1), 85–93. http://doi.org/10.1016/j.yebeh.2011.02.016

Brown, F. C., Westerveld, M., Langfitt, J. T., Hamberger, M., Hamid, H., Shinnar, S., … Spencer, S. S. (2014). Influence of anxiety on memory performance in temporal lobe epilepsy. *Epilepsy & Behavior*, *31*, 19–24. http://doi.org/10.1016/j.yebeh.2013.10.009

Butler, C. R., Bhaduri, A., Acosta-Cabronero, J., Nestor, P. J., Kapur, N., Graham, K. S., … Zeman, A. Z. (2008). Transient epileptic amnesia: regional brain atrophy and its relationship to memory deficits. *Brain*, *132*(2), 357–368. http://doi.org/10.1093/brain/awn336

Busch, R. M., Dulay, M. F., Kim, K. H., Chapin, J. S., Jehi, L., Kalman, C. C., ... & Najm, I. M. (2011). Pre-surgical mood predicts memory decline after anterior temporal lobe resection for epilepsy. *Archives of clinical neuropsychology*.

Caller, T. A., Secore, K. L., Ferguson, R. J., Roth, R. M., Alexandre, F. P., Henegan, P. L., … Jobst, B. C. (2015). Design and feasibility of a memory intervention with focus on self-management for cognitive impairment in epilepsy. *Epilepsy & Behavior*, *44*, 192–194. http://doi.org/10.1016/j.yebeh.2014.12.036

Cella, D., Nowinski, C., Peterman, A., Victorson, D., Miller, D., Lai, J.-S., & Moy, C. (2011). The Neurology Quality-of-Life Measurement Initiative. *Archives of Physical Medicine and Rehabilitation*, *92*(10), S28–S36. http://doi.org/10.1016/j.apmr.2011.01.025

Corcoran, R., & Thompson, P. (1993). Epilepsy and poor memory: who complains and what do they mean? *British journal of clinical psychology*,*32*(2), 199-208.

Cragar, D. E., Berry, D. T., Fakhoury, T. A., Cibula, J. E., & Schmitt, F. A. (2002). A review of diagnostic techniques in the differential diagnosis of epileptic and nonepileptic seizures. *Neuropsychology Review*, *12*(1), 31-64.

Cramer, J. A., Wang, Z. J., Chang, E., Powers, A., Copher, R., Cherepanov, D., & Broder, M. S. (2014). Healthcare utilization and costs in adults with stable and uncontrolled epilepsy. *Epilepsy & Behavior*, *31*, 356–362. http://doi.org/10.1016/j.yebeh.2013.09.046

Curt LaFrance Jr., W., Alosco, M. L., Davis, J. D., Tremont, G., Ryan, C. E., Keitner, G. I., … Blum, A. S. (2011). Impact of family functioning on quality of life in patients with psychogenic nonepileptic seizures versus epilepsy: Family Functioning, Quality of Life, and Seizures. *Epilepsia*, http://doi.org/10.1111/j.1528-1167.2010.02765.x

D'Alessio, L., Giagante, B., Oddo, S., Silva W, W., Solís, P., Consalvo, D., & Kochen, S. (2006). Psychiatric disorders in patients with psychogenic non-epileptic seizures, with and without comorbid epilepsy. *Seizure*, *15*(5), 333–339. http://doi.org/10.1016/j.seizure.2006.04.003

Dickinson, P., & Looper, K. J. (2012). Psychogenic nonepileptic seizures: A current overview: *PNES Review*. *Epilepsia*, *53*(10), 1679–1689. http://doi.org/10.1111/j.1528-1167.2012.03606.x

Dodrill, C. B. (2004). Neuropsychological effects of seizures. *Epilepsy & Behavior*, *5*, 21–24. http://doi.org/10.1016/j.yebeh.2003.11.004

Drane, D. L., Williamson, D. J., Stroup, E. S., Holmes, M. D., Jung, M., Koerner, E., … Miller, J. W. (2006). Cognitive Impairment Is Not Equal in Patients with Epileptic and Psychogenic Nonepileptic Seizures. *Epilepsia*, *47*(11), 1879–1886. http://doi.org/10.1111/j.1528-1167.2006.00611.x

Elixhauser, A., Leidy, N. K., Meador, K., Means, E., & Willian, M. K. (1999). The relationship between memory performance, perceived cognitive function, and mood in patients with epilepsy. *Epilepsy Research*, *37*(1), 13–24.

Elliott, J. O., Charyton, C., Sprangers, P., Lu, B., & Moore, J. L. (2011). The impact of marriage and social support on persons with active epilepsy. *Epilepsy & Behavior*, *20*(3), 533–538. http://doi.org/10.1016/j.yebeh.2011.01.013

Elliott, J. O., & Richardson, V. E. (2014). The biopsychosocial model and quality of life in persons with active epilepsy. *Epilepsy & Behavior*, *41*, 55–65. http://doi.org/10.1016/j.yebeh.2014.09.035

Fargo, J. D., Schefft, B. K., Szaflarski, J. P., Dulay, M. F., Marc Testa, S., Privitera, M. D., & Yeh, H.-S. (2004). Accuracy of self-reported neuropsychological functioning in individuals with epileptic or psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *5*(2), 143–150. http://doi.org/10.1016/j.yebeh.2003.11.023

Fiszman, A., Alves-Leon, S. V., Nunes, R. G., Isabella, D. A., & Figueira, I. (2004). Traumatic events and posttraumatic stress disorder in patients with psychogenic nonepileptic seizures: a critical review. *Epilepsy & Behavior*, *5*(6), 818-825.Flanagan, J. L., & Jackson, S. T. (1997). Test-retest reliability of three aphasia tests: Performance of non-brain-damaged older adults. *Journal of Communication Disorders, 30*(1), 33-43.

Fuerst, D., Shah, J., Shah, A., & Watson, C. (2003). Hippocampal sclerosis is a progressive disorder: a longitudinal volumetric MRI study. *Annals of neurology*, *53*(3), 413-416. Galer, S., Urbain, C., De Tiège, X., Emeriau, M., Leproult, R., Deliens, G., … Van Bogaert, P. (2015). Impaired sleep-related consolidation of declarative memories in idiopathic focal epilepsies of childhood. *Epilepsy & Behavior*, *43*, 16–23. http://doi.org/10.1016/j.yebeh.2014.11.032

Galioto, R., Blum, A. S., & Tremont, G. (2015). Subjective cognitive complaints versus objective neuropsychological performance in older adults with epilepsy. *Epilepsy & Behavior*, *51*, 48-52.Giovagnoli, A. R. (2013). Awareness, overestimation, and underestimation of cognitive functions in epilepsy. *Epilepsy & Behavior*, *26*(1), 75–80. http://doi.org/10.1016/j.yebeh.2012.11.001

Giovagnoli, A. R., & Avanzini, G. (2000). Quality of life and memory performance in patients with temporal lobe epilepsy. *Acta Neurologica Scandinavica*, *101*(5), 295–300.

Gordon, P. C., Valiengo, L. da C. L., Proença, I. C. G. F., Kurcgant, D., Jorge, C. L., Castro, L. H., & Marchetti, R. L. (2014). Comorbid epilepsy and psychogenic non-epileptic seizures: How well do patients and caregivers distinguish between the two. *Seizure*, *23*(7), 537–541. http://doi.org/10.1016/j.seizure.2014.04.002

Grewe, P., Lahr, D., Kohsik, A., Dyck, E., Markowitsch, H. J., Bien, C. G., … Piefke, M. (2014). Real-life memory and spatial navigation in patients with focal epilepsy: Ecological validity of a virtual reality supermarket task. *Epilepsy & Behavior*, *31*, 57–66. http://doi.org/10.1016/j.yebeh.2013.11.014

Gul, A., & Ahmad, H. (2014). Cognitive deficits and emotion regulation strategies in patients with psychogenic nonepileptic seizures: A task-switching study. *Epilepsy & Behavior*, *32*, 108–113. http://doi.org/10.1016/j.yebeh.2014.01.015

Hall, K. E., Isaac, C. L., & Harris, P. (2009). Memory complaints in epilepsy: An accurate reflection of memory impairment or an indicator of poor adjustment? A Review of the literature. *Clinical Psychology Review*, *29*(4), 354–367. http://doi.org/10.1016/j.cpr.2009.03.001

Heaton, R., Miller, S.W.., Taylor, M., & Grant, I. (2004). *Revised comprehensive norms for an expanded Halstead-Reitan Battery: Demographically adjusted neuropsychological norms for African American and Caucasian adults*. Lutz, Fl: Psychological Assessment Resources, Inc.

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

Helmstaedter, C., Kurthen, M., Lux, S., Reuber, M., & Elger, C. E. (2003). Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. .*Annals of neurology*, *54*(4), 425-432.

Hendriks, M. P. H., Aldenkamp, A. P., Van der Vlugt, H., Alpherts, W. C. J., & Vermeulen, J. (2002). Memory complaints in medically refractory epilepsy: relationship to epilepsy-related factors. *Epilepsy & Behavior*, *3*(2), 165-172.

Hermann, B., Seidenberg, M., Bell, B., Rutecki, P., Sheth, R. D., Wendt, G., ... & Magnotta, V. (2003). Extratemporal quantitative MR volumetrics and neuropsychological status in temporal lobe epilepsy. *Journal of the International Neuropsychological Society*, *9*(03), 353-362

Hermann, B., Seidenberg, M., & Jones, J. (2008). The neurobehavioural comorbidities of epilepsy: can a natural history be developed? *The Lancet Neurology*, *7*(2), 151–160.

Hermann, B., Seidenberg, M., Lee, E. J., Chan, F., & Rutecki, P. (2007). Cognitive phenotypes in temporal lobe epilepsy. *Journal of the International Neuropsychological Society*, *13*(01), 12-20.

Hermann, B., Seidenberg, M., Sager, M., Carlsson, C., Gidal, B., Sheth, R., … Asthana, S. (2008). Growing old with epilepsy: the neglected issue of cognitive and brain health in aging and elder persons with chronic epilepsy. *Epilepsia*, *49*(5), 731–740. http://doi.org/10.1111/j.1528-1167.2007.01435.x

Hernandez, M.-T., Sauerwein, H. C., Jambaqué, I., de Guise, E., Lussier, F., Lortie, A., … Lassonde, M. (2003). Attention, memory, and behavioral adjustment in children with frontal lobe epilepsy. *Epilepsy & Behavior*, *4*(5), 522–536. http://doi.org/10.1016/j.yebeh.2003.07.014

Herskovitz, M. (2015). Psychogenic nonepileptic seizure patterns in patients with epilepsy. *Psychosomatics*, *56*(1), 78–84.

Hill, S. W., & Gale, S. D. (2011). Neuropsychological characteristics of nonepileptic seizure semiological subgroups. *Epilepsy & Behavior*, *22*(2), 255–260. http://doi.org/10.1016/j.yebeh.2011.06.011

Hirsch, E., Schmitz, B., & Carreno, M. (2003). Epilepsy, antiepileptic drugs (AEDs) and cognition. *Acta Neurologica Scandinavica*, *108*(s180), 23–32.

Hoepner, R., Labudda, K., May, T. W., Schöndienst, M., Bien, C. G., & Brandt, C. (2014). Distinguishing between patients with pure psychogenic nonepileptic seizures and those with comorbid epilepsy by means of clinical data. *Epilepsy & Behavior*, *35*, 54–58. http://doi.org/10.1016/j.yebeh.2014.04.002

Hoppe, C., & Elger, C. E. (2011). Depression in epilepsy: a critical review from a clinical perspective. *Nature Reviews Neurology*, *7*(8), 462–472. http://doi.org/10.1038/nrneurol.2011.104

Hudson, J. M., Flowers, K. A., & Walster, K. L. (2014). Attentional control in patients with temporal lobe epilepsy. *Journal of Neuropsychology*, *8*(1), 140–146. http://doi.org/10.1111/jnp.12008

Institute of Medicine (U.S.), Committee on the Public Health Dimensions of the Epilepsies, & England, M. J. (2012). *Epilepsy across the spectrum promoting health and understanding*. Washington, D.C.: National Academies Press. Retrieved from http://site.ebrary.com/id/10594230

Janecek, J. K., Winstanley, F. S., Sabsevitz, D. S., Raghavan, M., Mueller, W., Binder, J. R., & Swanson, S. J. (2013). Naming outcome after left or right temporal lobectomy in patients with bilateral language representation by Wada testing. *Epilepsy & Behavior*, *28*(1), 95–98. http://doi.org/10.1016/j.yebeh.2013.04.006

Jones-Gotman, M., & Milner, B. (1977) Design fluency: The invention of nonsense drawings after focal cortical lesions. *Neuropsychologia, 15*, 653-674

Jungwirth, S., Fischer, P., Weissgram, S., Kirchmeyr, W., Bauer, P., & Tragl, K.-H. (2004). Subjective Memory Complaints and Objective Memory Impairment in the Vienna-Transdanube Aging Community. *Journal of the American Geriatrics Society*, *52*(2), 263–268.

Kalogjera-Sackellares, D., & Sackellares, J. C. (1999). Intellectual and neuropsychological features of patients with psychogenic pseudoseizures. *Psychiatry Research*, *86*(1), 73-84.

Karakis, I., Montouris, G. D., Piperidou, C., Luciano, M. S., Meador, K. J., & Cole, A. J. (2014). Patient and caregiver quality of life in psychogenic non-epileptic seizures compared to epileptic seizures. *Seizure*, *23*(1), 47–54. http://doi.org/10.1016/j.seizure.2013.09.011

Kemp, S., Illman, N. A., Moulin, C. J. A., & Baddeley, A. D. (2012). Accelerated long-term forgetting (ALF) and transient epileptic amnesia (TEA): Two cases of epilepsy-related memory disorder. *Epilepsy & Behavior*, *24*(3), 382–388. http://doi.org/10.1016/j.yebeh.2012.04.119

Kent, G. P., Schefft, B. K., Howe, S. R., Szaflarski, J. P., Yeh, H.-S., & Privitera, M. D. (2006). The effects of duration of intractable epilepsy on memory function. *Epilepsy & Behavior*, *9*(3), 469–477. http://doi.org/10.1016/j.yebeh.2006.07.005

Kobau, R., Cui, W., Kadima, N., Zack, M. M., Sajatovic, M., Kaiboriboon, K., & Jobst, B. (2014). Tracking psychosocial health in adults with epilepsy—Estimates from the 2010 National Health Interview Survey. *Epilepsy & Behavior*, *41*, 66–73. http://doi.org/10.1016/j.yebeh.2014.08.002

Korczyn, A. D., Schachter, S. C., Brodie, M. J., Dalal, S. S., Engel, J., Guekht, A., ... & Mares, P. (2013). Epilepsy, cognition, and neuropsychiatry (Epilepsy, Brain, and Mind, part 2). *Epilepsy & Behavior*, *28*(2), 283-302.Kwan, P., & Brodie, M. J. (2001). Neuropsychological effects of epilepsy and antiepileptic drugs. *The Lancet*, *357*(9251), 216-222.

Lahr, D., Beblo, T., & Hartje, W. (2007). Cognitive performance and subjective complaints before and after remission of major depression. *Cognitive neuropsychiatry*, *12*(1), 25-45.Lai, J.-S., Nowinski, C. J., Zelko, F., Wortman, K., Burns, J., Nordli, D. R., & Cella, D. (2015). Validation of the Neuro-QoL measurement system in children with epilepsy. *Epilepsy & Behavior*, *46*, 209–214. http://doi.org/10.1016/j.yebeh.2015.02.038

Lesser, R. P. (2003). Treating psychogenic nonepileptic seizures: Easier said than done. *Annals of Neurology*, *53*(3), 285–286. http://doi.org/10.1002/ana.10542

Liik, M., Vahter, L., Gross-Paju, K., & Haldre, S. (2009). Subjective complaints compared to the results of neuropsychological assessment in patients with epilepsy: The influence of comorbid depression. *Epilepsy Research*, *84*(2-3), 194–200. http://doi.org/10.1016/j.eplepsyres.2009.02.006

Lineweaver, T. T., Naugle, R. I., Cafaro, A. M., Bingaman, W., & Lüders, H. O. (2004). Patients' perceptions of memory functioning before and after surgical intervention to treat medically refractory epilepsy. *Epilepsia*, *45*(12), 1604–1612.

Lin, J. J., Mula, M., & Hermann, B. P. (2012). Uncovering the neurobehavioural comorbidities of epilepsy over the lifespan. *The Lancet*, *380*(9848), 1180–1192.

Longo, C. A., Kerr, E. N., & Smith, M. L. (2013). Executive functioning in children with intractable frontal lobe or temporal lobe epilepsy. *Epilepsy & Behavior*, *26*(1), 102–108. http://doi.org/10.1016/j.yebeh.2012.11.003

Loughman, A., Bowden, S. C., & D'Souza, W. (2014). Cognitive functioning in idiopathic generalised epilepsies: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *43*, 20–34. http://doi.org/10.1016/j.neubiorev.2014.02.012

Lou Smith, M., Elliott, I. M., & Lach, L. (2006). Memory outcome after pediatric epilepsy surgery: Objective and subjective perspectives. *Child Neuropsychology*, *12*(3), 151–164. http://doi.org/10.1080/09297040591001076

MacAllister, W. S., Bender, H. A., Whitman, L., Welsh, A., Keller, S., Granader, Y., & Sherman, E. M. (2012). Assessment of executive functioning in childhood epilepsy: the Tower of London and BRIEF. *Child Neuropsychology*, *18*(4), 404-415.

Magaudda, A., Gugliotta, S. C., Tallarico, R., Buccheri, T., Alfa, R., & Laganà, A. (2011). Identification of three distinct groups of patients with both epilepsy and psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *22*(2), 318–323. http://doi.org/10.1016/j.yebeh.2011.07.005

Marinas, A., Elices, E., Gil-Nagel, A., Salas-Puig, J., Sánchez, J. C., Carreño, M., … Serratosa, J. M. (2011). Socio-occupational and employment profile of patients with epilepsy. *Epilepsy & Behavior*, *21*(3), 223–227. http://doi.org/10.1016/j.yebeh.2011.01.025

Marino, S. E., Meador, K. J., Loring, D. W., Okun, M. S., Fernandez, H. H., Fessler, A. J., … Werz, M. A. (2009). Subjective perception of cognition is related to mood and not performance. *Epilepsy & Behavior*, *14*(3), 459–464. http://doi.org/10.1016/j.yebeh.2008.12.007

Marques, C. M., Caboclo, L. O. S. F., da Silva, T. I., da Silva Noffs, M. H., Carrete, H., Lin, K., … Yacubian, E. M. T. (2007). Cognitive decline in temporal lobe epilepsy due to unilateral hippocampal sclerosis. *Epilepsy & Behavior*, *10*(3), 477–485. http://doi.org/10.1016/j.yebeh.2007.02.002

Meador, K. J. (2002). Cognitive outcomes and predictive factors in epilepsy.*Neurology*, *58*(8 suppl 5),

Meneses, R. F., Pais-Ribeiro, J. L., da Silva, A. M., & Giovagnoli, A. R. (2009). Neuropsychological predictors of quality of life in focal epilepsy. *Seizure*, *18*(5), 313–319. http://doi.org/10.1016/j.seizure.2008.11.010

Milberg, W., Greiffenstein, M., Lewis, R., & Rourke, D. (1980). Differentiation of temporal lobe and generalized seizure patients with the WAIS. *Journal of Consulting and Clinical Psychology*, *48*(1), 39.

Mitchell, A. J., Kemp, S., Benito-LeÃ^{3}n, J., & Reuber, M. (2010). The influence of cognitive impairment on health-related quality of life in neurological disease. *Acta Neuropsychiatrica*, *22*(1), 2–13. http://doi.org/10.1111/j.1601-5215.2009.00439.x

Motamedi, G., & Meador, K. (2003). Epilepsy and cognition. *Epilepsy & Behavior*, *4*, 25–38. http://doi.org/10.1016/j.yebeh.2003.07.004

Mula, M., & Trimble, M. R. (2009). Antiepileptic drug-induced cognitive adverse effects. *CNS Drugs*, *23*(2), 121–137.

Myers, L., Lancman, M., Laban-Grant, O., Matzner, B., & Lancman, M. (2012). Psychogenic non-epileptic seizures: Predisposing factors to diminished quality of life. *Epilepsy & Behavior*, *25*(3), 358–362. http://doi.org/10.1016/j.yebeh.2012.08.024

Nowinski, C. J., Victorson, D., Cavazos, J. E., Gershon, R., & Cella, D. (2010). Neuro-QOL and the NIH Toolbox: implications for epilepsy. *Therapy*, *7*(5), 533–540.

O'Brien, F. M., Fortune, G. M., Dicker, P., O'Hanlon, E., Cassidy, E., Delanty, N., … Murphy, K. C. (2015). Psychiatric and neuropsychological profiles of people with psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *43*, 39–45. http://doi.org/10.1016/j.yebeh.2014.11.012

O'shea, M. F., Saling, M. M., Bladin, P. F., & Berkovic, S. F. (1996). Does naming contribute to memory self-report in temporal lobe epilepsy? *Journal of clinical and experimental neuropsychology*, *18*(1), 98-109.

Oyegbile, T. O., Dow, C., Jones, J., Bell, B., Rutecki, P., Sheth, R., … Hermann, B. P. (2004). The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. *Neurology*, *62*(10), 1736–1742. http://doi.org/10.1212/01.WNL.0000125186.04867.34

Pais-Ribeiro, J., da Silva, A. M., Meneses, R. F., & Falco, C. (2007). Relationship between optimism, disease variables, and health perception and quality of life in individuals with epilepsy. *Epilepsy & Behavior, 11*(1), 33–38. http://doi.org/10.1016/j.yebeh.2007.04.010

Piazzini, A., Beghi, E., Turner, K., & Ferraroni, M. (2008). Health-related quality of life in epilepsy: Findings obtained with a new Italian instrument. *Epilepsy & Behavior*, *13*(1), 119–126. http://doi.org/10.1016/j.yebeh.2008.02.017

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

Prigatano, G. P., & Kirlin, K. A. (2009). Self-appraisal and objective assessment of cognitive and affective functioning in persons with epileptic and nonepileptic seizures. *Epilepsy & Behavior*, *14*(2), 387–392. http://doi.org/10.1016/j.yebeh.2008.12.001

Rayner, G., Wrench, J. M., & Wilson, S. J. (2010). Differential contributions of objective memory and mood to subjective memory complaints in refractory focal epilepsy. *Epilepsy & Behavior*, *19*(3), 359-364.

Reeve, B. B., Burke, L. B., Chiang, Y. P., Clauser, S. B., Colpe, L. J., Elias, J. W., ... & Moy, C. S. (2007). Enhancing measurement in health outcomes research supported by Agencies within the US Department of Health and Human Services. *Quality of life Research*, *16*(1), 175-186.

Ross, T. P. (2014). The reliability and convergent and divergent validity of the Ruff Figural Fluency Test in healthy young adults. *Archives Of Clinical Neuropsychology*, *29*(8), 806-817. doi:10.1093/arclin/acu052

Quigg, M., Armstrong, R. F., Farace, E., & Fountain, N. B. (2002). Quality of life outcome is associated with cessation rather than reduction of psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *3*(5), 455–459.

Quintas, R., Raggi, A., Giovannetti, A. M., Pagani, M., Sabariego, C., Cieza, A., & Leonardi, M. (2012). Psychosocial difficulties in people with epilepsy: A systematic review of literature from 2005 until 2010. *Epilepsy & Behavior*, *25*(1), 60–67. http://doi.org/10.1016/j.yebeh.2012.05.016

Reuber, M. (2008). Psychogenic nonepileptic seizures: Answers and questions. *Epilepsy & Behavior*, *12*(4), 622–635. http://doi.org/10.1016/j.yebeh.2007.11.006

Reuber, M., & Elger, C. E. (2003). Psychogenic nonepileptic seizures: review and update. *Epilepsy & Behavior*, *4*(3), 205-216.

Reuber, M., Fernandez, G., Helmstaedter, C., Qurishi, A., & Elger, C. E. (2002). Evidence of brain abnormality in patients with psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *3*(3), 249–254.

Rayner, G., Wrench, J. M., & Wilson, S. J. (2010). Differential contributions of objective memory and mood to subjective memory complaints in refractory focal epilepsy. *Epilepsy & Behavior*, *19*(3), 359–364. http://doi.org/10.1016/j.yebeh.2010.07.019

Rösche, J., Kundt, G., Weber, R., Fröscher, W., & Uhlmann, C. (2012). Memory deficits and depression in patients with chronic epilepsy. *Acta Neuropsychiatrica*, *24*(4), 230–235. http://doi.org/10.1111/j.1601-5215.2011.00625.x

Rudzinski, L. A., & Meador, K. J. (2013). Epilepsy and neuropsychological comorbidities. *CONTINUUM: Lifelong Learning in Neurology*, *19*(3, Epilepsy), 682–696.

Ruff, R. M., Light, R. H., & Evans, R. W. (1987). The Ruff Figural Fluency Test: a normative study with adults. *Developmental Neuropsychology*, *3*(1), 37-51.

Salas-Puig, J., Gil-Nagel, A., Serratosa, J. M., Sánchez-Alvarez, J. C., Elices, E., Villanueva, V., ... & Porcel, J. (2009). Self-reported memory problems in everyday activities in patients with epilepsy treated with antiepileptic drugs. *Epilepsy & Behavior*, *14*(4), 622-627.

Sánchez-Cubillo, I., PeriáñEz, J. A., Adrover-Roig, D., RodríGuez-SáNchez, J. M., RíOs-Lago, M., Tirapu, J., & Barceló, F. (2009). Construct validity of the Trail Making Test: Role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. *Journal of the International Neuropsychological Society*, *15*(03), 438. http://doi.org/10.1017/S1355617709090626

Samarasekera, S. R., Helmstaedter, C., & Reuber, M. (2015). Cognitive impairment in adults with epilepsy: The relationship between subjective and objective assessments of cognition. *Epilepsy & Behavior*, *52*, 9-13.

Schoenberg, M. R., Werz, M. A., & Drane, D. L. (2011). Epilepsy and Seizures. In M. R. Schoenberg & J. G. Scott (Eds.), *The little black book of neuropsychology* (pp. 423–520). Boston, MA: Springer US. Retrieved from http://link.springer.com/10.1007/978-0-387-76978-3_16

Smeets, V. M. J., van Lierop, B. A. G., Vanhoutvin, J. P. G., Aldenkamp, A. P., & Nijhuis, F. J. N. (2007). Epilepsy and employment: Literature review. *Epilepsy & Behavior*, *10*(3), 354–362. http://doi.org/10.1016/j.yebeh.2007.02.006

Stern, R. A., & White, T. (2003). *NAB, Neuropsychological Assessment Battery: Attention Module Stimulus Book. Form 2*. Psychological Assessment Resources.

Strutt, A. M., Hill, S. W., Scott, B. M., Uber-Zak, L., & Fogel, T. G. (2011). A comprehensive neuropsychological profile of women with psychogenic nonepileptic seizures. *Epilepsy & Behavior*, *20*(1), 24–28. http://doi.org/10.1016/j.yebeh.2010.10.004

Szaflarski, J. P., Hughes, C., Szaflarski, M., Ficker, D. M., Cahill, W. T., Li, M., & Privitera, M. D. (2003). Quality of life in psychogenic nonepileptic seizures. *Epilepsia*, *44*(2), 236-242.

Szemere, E., & Jokeit, H. (2015). Quality of life is social – Towards an improvement of social abilities in patients with epilepsy. *Seizure*, *26*, 12–21. http://doi.org/10.1016/j.seizure.2014.12.008

Tramoni, E., Felician, O., Barbeau, E. J., Guedj, E., Guye, M., Bartolomei, F., & Ceccaldi, M. (2011). Long-term consolidation of declarative memory: insight from temporal lobe epilepsy. *Brain*, *134*(3), 816–831. http://doi.org/10.1093/brain/awr002

Turner, K., Piazzini, A., Chiesa, V., Barbieri, V., Vignoli, A., Gardella, E., … Gambini, O. (2011). Patients with epilepsy and patients with psychogenic non-epileptic seizures: Video-EEG, clinical and neuropsychological evaluation. *Seizure*, *20*(9), 706–710. http://doi.org/10.1016/j.seizure.2011.07.001

Uijl, S. G., Uiterwaal, C. S. M. P., Aldenkamp, A. P., Carpay, J. A., Doelman, J. C., Keizer, K., … van Donselaar, C. A. (2006). A cross-sectional study of subjective complaints in patients with epilepsy who seem to be well-controlled with anti-epileptic drugs. *Seizure*, *15*(4), 242–248. http://doi.org/10.1016/j.seizure.2006.02.009

Velissaris, S. L., Wilson, S. J., Newton, M. R., Berkovic, S. F., & Saling, M. M. (2009). Cognitive complaints after a first seizure in adulthood: Influence of psychological adjustment. *Epilepsia*, *50*(5), 1012–1021. http://doi.org/10.1111/j.1528-1167.2008.01893.x

Victorson, D., Cavazos, J. E., Holmes, G. L., Reder, A. T., Wojna, V., Nowinski, C., … Cella, D. (2014). Validity of the Neurology Quality-of-Life (Neuro-QoL) measurement system in adult epilepsy. *Epilepsy & Behavior*, *31*, 77–84. http://doi.org/10.1016/j.yebeh.2013.11.008

Wechsler, D., (2009). *Advanced clinical solutions for the WAIS-IV and WMS-IV*. San Antonio, TX: Pearson.

Whitehead, K., Kandler, R., & Reuber, M. (2013). Patients' and neurologists' perception of epilepsy and psychogenic nonepileptic seizures. *Epilepsia*, *54*(4), 708–717. http://doi.org/10.1111/epi.12087

Wilner, A. N., Sharma, B. K., Thompson, A., Soucy, A., & Krueger, A. (2014). Diagnoses, procedures, drug utilization, comorbidities, and cost of health care for people with epilepsy in 2012. *Epilepsy & Behavior*, *41*, 83–90. http://doi.org/10.1016/j.yebeh.2014.08.131

Wiseman, H., & Reuber, M. (2015). New insights into psychogenic nonepileptic seizures 2011–2014. *Seizure*, *29*, 69-80.

Witt, J.-A., Glöckner, C., & Helmstaedter, C. (2012). Extended retention intervals can help to bridge the gap between subjective and objective memory impairment. *Seizure*, *21*(2), 134–140. http://doi.org/10.1016/j.seizure.2011.10.007

World Health Organization, & WHO Collaborating Centre for International Drug Monitoring. (2002). *The importance of pharmacovigilance.* [Geneva]: World Health Organization : Uppsala Monitoring Centre, WHO Collaborating Centre for International Drug Monitoring.

Yochim, B. P., Kane, K. D., & Mueller, A. E. (2009). Naming Test of the Neuropsychological Assessment Battery: Convergent and Discriminant Validity. *Archives of Clinical Neuropsychology*, *24*(6), 575–583. http://doi.org/10.1093/arclin/acp053