

THE NEUROPSYCHOLOGICAL ASSESSMENT BATTERY (NAB): A TEST OF
CRITERION VALIDITY WITHIN AN EPILEPSY POPULATION

By

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This dissertation is dedicated, in loving memory, to Donna Graham.

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Abstract of Dissertation Presented to the Graduate School
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This study attempted to assess the clinical utility of the Neuropsychological Assessment Battery (NAB) within an epilepsy population by analyzing how well NAB scores (as well as specific additional variables derived from NAB scores) predicted lateralization and localization of seizure focus in our sample. Forty-five participants with documented or suspected epilepsy were tested while undergoing 24-hour video electroencephalographic (V-EEG) monitoring during their stay as an inpatient in the epilepsy monitoring unit (EMU) at UF/Shands Hospital in Gainesville, Florida over a 16 month period. Each participant was administered the NAB Screening Module as well as the five Core NAB Modules (Attention, Language, Memory, Spatial, and Executive Functions).

Of the 45 participants tested, twenty were found to have electrographic seizures (four left lateralized, eleven right lateralized, and five nonlateralized), twelve were found to have psychogenic non-epileptic seizures (PNES), and thirteen subjects had no clinical events during their stay and were therefore unable to be definitively diagnosed or classified.

The results of our study provided some support for the clinical utility of the NAB within an epilepsy population. Specifically, our results suggested that certain combinations of NAB scores

(as well as additional derived scores) were able to discriminate between individuals with temporal lobe epilepsy and individuals whose seizures do not originate in the temporal lobe at a rate greater than chance. Our results provided limited evidence, however, for the NAB's ability to successfully predict seizure laterality (from which cerebral hemisphere seizures originate). This may be due to the NAB's limited sensitivity with regard to this factor, although other sample-specific constraints may have also played a role in this limitation. Future research with the NAB (specifically, tests of the NAB's ability to predict lateralization and localization of seizure focus when the results are analyzed by one or more trained clinical neuropsychologists, similar to the techniques used in current practice with this population using other neuropsychological batteries) is warranted to more definitively determine its clinical utility within an epilepsy population.

CHAPTER ONE INTRODUCTION

The Neuropsychological Assessment Battery (NAB) “is a comprehensive, modular battery of neuropsychological tests developed for the assessment of a wide array of cognitive skills and functions in adults aged 18 years to 97 years, with known or suspected disorders of the central nervous system” (Stern & White, 2003, p.1). The NAB has many putative advantages over other comprehensive neuropsychological batteries such as the Halstead-Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1993) and the Luria-Nebraska Neuropsychological Battery (Golden, Purisch, & Hammeke, 1985), including its significantly abbreviated administration time. It is estimated that all six Modules of the NAB (including the five Core Modules and the Screening Module) can be administered in less than four hours, nearly half the time it takes to administer the complete Halstead-Reitan Battery. With an emphasis on increasing cost-effectiveness of assessment services, the NAB offers an attractive alternative to established neuropsychological approaches by allowing for a reasonably comprehensive neuropsychological assessment that can be conducted in a relatively short amount of time.

Neuropsychological Assessment Battery (NAB) Features

Major features of the NAB compared to other comprehensive neuropsychological batteries include its resilience to floor and ceiling effects, modifiable modes of use as both a flexible and a fixed battery, comprehensive coverage of all functional domains, use of a single standardization group for the entire battery, availability of alternate forms and demographically-corrected norms, ease of utility for both the administrator and patient, and a particular focus on the inclusion of ecologically valid tasks (Stern & White, 2003). An example of efforts to provide more ecologically valid assessments is found in the digits backward task, a formal test of attention and working memory abilities that requires the subject to repeat back a series of orally presented

numbers in backwards order. Digits backwards is a commonly used task in neuropsychological assessment batteries (including the NAB), and although this task provides relevant information, it can do little by itself to predict impairment in functioning in a real-world situation as the requirements of the task itself are not commonly found in everyday life. In contrast, in addition to assessing attention and working memory with a digits backward task, the NAB also includes a Driving Scenes Task, a test of attention in which the subject briefly views a drawing of a driving scene as shown from behind the wheel of a motor vehicle. The subject is then shown a different scene and required to point out the changes that occurred between the two scenes (Stern & White, 2003). A recent publication examined the ability of Driving Scenes subtest performance to classify groups of normal and mildly demented subjects into driving categories. All subjects were administered the driving scenes subtest of the NAB, as well as the “useful field of view” (UFOV; Owsley et al., 1991) test and a comprehensive road course driving test. After performing a discriminant function analysis on the results, it was determined that the Driving Scenes score could be used to correctly classify subjects into their global ratings of driving ability (rated as safe, marginal, or unsafe), approximately 66% of the time (Brown et al., 2005). This is merely one example; in fact, the NAB contains at least one Daily Living subtest in each of its five Modules that “is designed to be congruent with an analogous real-world behavior” (White & Stern, 2003, p.7). For a full list of tests included in the NAB, see Table 1-1.

NAB Scores

Administration of the NAB provides scores that can be compared to either demographically corrected norms based on a national sample of 1,448 adults or to an alternative age-based, U.S. census-matched norm set based on a sample of 950 adults. Typical administration during clinical practice involves first administering the NAB Screening Module. Upon successful administration and scoring of the Screening Module, five Screening Domain

scores, as well as a Screening Total score, would be available for interpretation. The NAB was designed such that the Screening Domain scores would inform the examiner which subsequent full Domain Modules would be useful to administer. This design was structured to have dual-screening capabilities, such that individuals performing significantly poorly or significantly well on a given Screening Domain score would not have the full Module from that Domain administered to them. The rationale for this approach is that administering the full Domain Module to these individuals would essentially be pointless as they would likely perform at floor during the full Module (much as they did on the briefer Screening Domain) or would be equally uninformative as the person's performance on the Screening Domain Module was so high that they are clearly unimpaired in that particular Domain (Stern & White, 2003). In general, Domain scores on the NAB Screening Module below a Standard Score value of 74 to 75 or above a Standard Score value of 114 to 126 will indicate that further testing in that Domain is not needed. According to Table 1.10 of the NAB Administration, Scoring, and Interpretation Manual (Stern & White, 2003), the sensitivity of the NAB Screening Domain scores ranged from .95 to .96, while specificity ranged from .03 to .75. Specificity levels were lower for the Above Average cutoffs than the Moderately-to-Severely-Impaired cutoffs. The overall correct classification rate was .95 for the Moderately-to-Severely Impaired cutoffs and ranged from .67 to .79 for the Above Average cutoff.

Although the NAB offers significant data on the reliability and stability of the battery, as well as comprehensive sets of both demographically-corrected and age-based norms (Stern & White, 2003), there have been few validity studies assessing the utility of the NAB during clinical assessments with special populations (e.g., patients with epilepsy, Parkinson's disease, dementia, etc) or with specific referral questions to which neuropsychological assessments are

typically applied. In practice, the NAB and other neuropsychological instruments are often used to make specialized decisions, such as whether or not to offer surgery, medical, or rehabilitative treatment, or to determine whether a treatment has been beneficial or detrimental to neurocognitive function. To date, the studies that have been conducted to assess the validity of the NAB have variably supported its validity as a clinical instrument. However, these studies have focused primarily on assessing the validity of the NAB Screening Module alone (Grohman & Fals-Stewart, 2004; Iverson, Williamson, Ropacki, & Reilly, 2007; Temple, Zgalijardic, Abreu, Seale, Ostir, & Ottenbacher, 2009; Zgalijardic & Temple, 2010), the validity of one particular subtest or group of subtests of the NAB on predicting specific impairment (Brown et al., 2005; Cahn-Weiner, Wittenberg, & McDonald, 2009; Gavett et al., 2009; Yochim, Kane, & Mueller, 2009), or establishing base rates for low NAB scores in older adults (Brooks, Iverson, & White, 2007; Brooks, Iverson, & White, 2009). Thus far, limited data is available on the validity of the full NAB battery as a clinically relevant neuropsychological tool. The purpose of our study was to conduct a validity study on the use of the NAB in neurocognitive evaluations of patients with documented or suspected epilepsy.

Test Validation

There are a number of formal ways in which new psychometric tests may be validated. Some of the most common types of test validity include construct validity, predictive validity, concurrent validity, and discriminant validity. According to Anastasi & Urbina (1997), construct validity is generally defined as a test's ability to measure the underlying construct or ability it is attempting to measure. Demonstration of construct validity depends on showing that the test correlates highly with validated measure(s) of the same theoretical construct (convergent validity), and shows lower correlations with measures of different constructs (discriminant validity; Campbell & Fiske, 1959; Anastasi & Urbina, 1997). Criterion-oriented validity refers to

a test's ability to predict outcome on some external outcome measure (such as when the score on a neuropsychological test is used to predict the presence of a localized brain lesion). When the test is shown to predict some criterion available later in time, it is shown to demonstrate "predictive validity". When the criterion is available at the same time as the test score, the test shows "concurrent" validity. The present study attempts to establish the concurrent validity of the NAB in lateralizing and localizing seizure focus in a surgical epilepsy population, since neuropsychological test scores, neuroimaging findings, and electrographic localization data all result from the same interdisciplinary workup.

Epilepsy

Epilepsy is "a common neurological disorder characterized by sudden, brief attacks that may alter motor activity, consciousness, and sensory experiences" (Snyder & Nussbaum, 1998, p. 304). Approximately two million Americans have epilepsy, with nearly 125,000 new cases of epilepsy being diagnosed each year (Abel, 2005). The most common treatments for epilepsy involve the use of anti-epileptic drugs (AEDs). Some other forms of treatment may also involve the patient following a ketogenic diet, or the implantation of a Vagus nerve stimulator (Mayo Clinic, 2007). Unfortunately, as many as 35% of patients with epilepsy have drug-resistant, or intractable, epilepsy (Abel, 2005). In some intractable cases of epilepsy in which a patient's seizures are not eliminated with AEDs or other common treatments, resective surgery to remove neural tissue at the site of seizure onset may be considered. In 1992, Pilcher, Lochareernkul, Primrose, Ojermann, and Ojermann estimated that as many as 1,000 resective seizure surgeries are conducted in the U.S. per year. With newer advancements in the field of neuroimaging to assist in determining seizure focus, it is likely that the number of resective seizure surgeries conducted in the U.S. has increased significantly since that time, with nearly 100 of these surgeries conducted at the Cleveland Clinic in 2007 alone (Cleveland Clinic, 2007).

However, there are many risks associated with resective brain surgery, including medical complications and neuropsychological morbidity. In 1957, Scoville and Milner published the first account of the famous patient, H.M., who developed a severe permanent anterograde amnesia following a bilateral anterior temporal lobectomy in an attempt to eliminate his seizures. His case raised awareness of surgery-induced neuropsychological morbidity, and today candidates for epilepsy surgery must undergo a wide variety of neuropsychological and neurological tests (e.g., electroencephalograph [EEG], magnetic resonance imaging [MRI], Wada) in order to ensure that losses to vital functions such as memory, motor function, vision, and language are minimized and that surgery will not place the patient at risk for developing functionally significant memory or language deficits (Valton & Mascott, 2004).

Before epilepsy surgery is performed, a candidate is typically admitted to the hospital for noninvasive (Phase I) monitoring, during which patients undergo neurological testing, 24-hour video EEG monitoring with scalp electrodes, and structural neuroimaging with specialized MRI protocols (Abel, 2005). In addition, the patient also often undergoes comprehensive neuropsychological assessment in order to further predict lateralization and localization of seizure focus. During this neuropsychological assessment, patients typically undergo a neuropsychological test battery that broadly evaluates functional domains including intellectual ability, language, executive functioning, material-specific memory functioning, visuo-perceptual/visuo-constructional skills, and motor functioning. During Phase I epilepsy monitoring, the patient is removed from their AEDs and may be subjected to sleep deprivation (a common epileptic trigger) in the hopes of eliciting seizure activity that can be monitored in order to best lateralize and localize the patient's seizure focus. As the nature of this type of hospitalization can be quite stressful on the patient, the importance of quick and efficient

methods of neuropsychological evaluation is vital. The advent of briefer neurocognitive batteries (like the NAB) thus has potential for improving the cost-effectiveness of clinical neuropsychological evaluation in this setting.

Non-Epileptic Seizures (NES)

Some patients seen within the context of clinical practice that are believed to have epilepsy are later found to have non-epileptic seizures (NES). There are two types of non-epileptic seizures, physiologic and psychogenic (Benbadis, 2005). Physiologic non-epileptic seizures are the result of a disruption of brain function due to physical causes other than true epilepsy, such as syncope, hypoglycemia, delirium tremens following alcohol abuse or eclampsia as a complication of pregnancy (Benbadis, 2010). In contrast, psychogenic non-epileptic seizures (PNES), which are sometimes erroneously called “pseudoseizures”, are episodes that appear to be seizure-like in regards to observable behavior yet are psychological in nature (often conceptualized as sharing similarities with conversion disorders) and, unlike physiological non-epileptic seizures, do not involve the characteristic electrical discharges associated with epilepsy. It is estimated that 20 to 30% of patients seen in epilepsy clinics are eventually diagnosed with psychogenic non-epileptic seizures (Martin, 2005). Approximately 75% of patients diagnosed with PNES are female, and PNES patients often tend to have additional psychological problems and diagnoses, comorbidities including fibromyalgia or chronic pain, and/or previous histories of abuse (Benbadis, 2005).

Although suspicions of psychogenic non-epileptic seizures may be raised following clinical interview in an epilepsy clinic, a definitive diagnosis of PNES is usually withheld until after a patient has undergone 24-hour video EEG monitoring. Whereas in genuine epilepsy this type of monitoring is useful in determining lateralization and localization of seizure focus, in PNES, it can be used to definitively *rule out* the presence of electrographic abnormalities during

observed behavioral events, and can provide evidence of behavioral inconsistencies in presentation between such patients and individuals with genuine epilepsy.

Previous Related Studies

The current study is related to a previously published study from our lab conducted by David Moser (Moser et al., 2000). Moser and his colleagues sought to compare the utility of EEG, MRI, and neuropsychological data in predicting the lateralization and localization of seizure focus in presurgical epilepsy patients. For the purpose of their study, EEG data consisted of a seizure lateralization index (SLI), which gave a measure of laterality along a continuum from -1 (purely left lateralized) to +1 (purely right lateralized). The SLI, and how it is calculated, will be discussed in more detail later as it will play an important role as a criterion in the current study. MRI data was quantified as left-right differences in hippocampal volume, and neuropsychological data was compiled from a number of tests administered to the patient as part a standard approach to presurgical neuropsychological evaluations at the University of Florida. In what follows, this battery is referred to as the UF standard neuropsychological battery, or SNB (See Table 1-2 for a full list of tests administered in the SNB). After the neuropsychological tests were administered, specific Domain scores (e.g., verbal memory, nonverbal memory, language, visuoconstruction, and motor) were calculated. For each functional domain (language, memory, etc.), demographically corrected scores on constituent tests were converted to a common z-score metric and averaged (by adding up the z-scores and dividing by the total number of tests included in that Domain) to derive overall Domain scores. These Domain scores, as well as the aforementioned EEG seizure lateralization index and difference in hippocampal volume (DHF) found from the MRI were entered, both separately and in various combinations, into leave-one-out (also called “Jackknife”) discriminant function analyses to evaluate their ability to predict left- vs. right-temporal lobe seizure lateralization. Subjects were

44 right-handed adult patients who “ultimately underwent successful anterior temporal lobectomy” (defined by seizure freedom after two years; Moser et al., 2000, p. 707). The authors found that EEG data alone correctly lateralized patients 89% of the time, whereas MRI data alone correctly lateralized patients 86% of the time. Neuropsychological data alone was able to correctly lateralize patients 66% of the time. Using all three in combination with each other improved the accuracy of lateralization prediction to 95%. From this data it becomes clear that the combination of EEG, MRI, and neuropsychological data serve as an excellent predictor of laterality in populations of individuals who ultimately undergo anterior temporal lobectomy (ATL). It is known that presurgical neuropsychological evaluation is valuable in predicting post-surgical outcome, provided that it correctly localizes the lesion. However, it could be argued that a full-day neuropsychological examination, which costs \$1,500, added relatively little to prediction and could be eliminated in a cost-effective environment. Developing shorter, more cost-effective approaches to presurgical neuropsychological assessment might be useful to tip that equation in a more favorable direction that would support the use of neuropsychological assessment as an integral part of standard epilepsy care.

The previous study has two notable limitations. The patients included in the study were all patients who eventually underwent surgery for their epilepsy. Therefore, the criterion variable which Moser and his colleagues used for group prediction was final data on which hemisphere was ultimately removed surgically. The first problem is that neuropsychological examination results contributed to the surgical decision and were thus not independent of patient classification. Also, in order for an intensive surgical procedure such as an ATL to be conducted, doctors must be highly confident in the lateralization and localization of seizure onset in a single hemisphere. In the Moser et al. study, of the 26 patients who underwent left ATL

surgery, the mean SLI score was $-.83$ (indicating moderately strong left lateralization). Of the 18 patients who underwent right ATL surgery, the mean SLI score was $.63$. Thus, in both groups of patients the SLI scores tend to be at the farther ends of the spectrum, representing more classical cases of lateralization. What is unclear is whether neuropsychological examination would have commanded more variance in situations in which the patient's seizure disorder was less firmly lateralized or in which all or some of the patients' events were nonepileptic. The consecutive admission design of our study allowed an evaluation of this possibility.

Hypotheses

Our study evaluated the validity and utility of the Neuropsychological Assessment Battery (NAB) in predicting the lateralization and localization of seizure focus in a sample of individuals with documented or suspected epilepsy by comparing the results of the NAB battery to numerical lateralization and localization data available from noninvasive inpatient video EEG. We attempted to address this by posing two primary research questions:

Question One

The first question related solely to lateralization of seizure focus. We examined how accurately NAB data predicted membership in one of three groups (left lateralized epilepsy, right lateralized epilepsy, and nonlateralized epilepsy/PNES) using SLI data as the criterion measure. At first glance, it may seem confusing why individuals with genuine but nonlateralizing epilepsy (such as individuals with generalized seizures) would be included in the same group as individuals diagnosed with PNES. The reason for this decision was that, within the context of an epilepsy clinical practice, future treatment options for both of these patient populations would not include respective seizure surgery, whereas individuals diagnosed with intractable epilepsy and found to be highly lateralized to the left or right hemisphere with regards to seizure focus may in fact eventually undergo such surgery. In order to determine group membership, the

scores obtained on the SLI in our sample were used. After the base rates of occurrence for each of the three categories within the current population sample were determined, a discriminant function analysis was conducted to examine how well specific NAB scores predicted group membership. Of primary interest were two construct scores that were derived from the Memory Module of the NAB, Verbal Memory and Nonverbal Memory. The NAB Memory Module consists of four primary subtests, including List Learning, Story Learning, Shape Learning, and Daily Living Memory subtests. The List Learning subtest and Story Learning subtests are entirely verbal memory tasks (See Table 1-1 for test descriptions), whereas the Shape Learning subtest is a nonverbal memory task. The Daily Living task was not included in the analysis because it contains both verbal and nonverbal components. In order to calculate these construct scores, methods consistent with those in the Moser et al. (2000) study were conducted. A Verbal Memory construct score was calculated by averaging z-scores obtained on the List Learning List A Long Delayed Recall task (from the List Learning subtest) and the Story Learning Phrase Unit Delayed Recall task (from the Story Learning subset). A Nonverbal Memory construct score was based upon the obtained z-score for their performance on the Shape Learning Delayed Recognition task of the Shape Learning subtest. As only one subtest was included in the Nonverbal Memory construct score, no mathematical averaging was necessary.

Once the Verbal Memory and Nonverbal Memory construct scores were calculated, they, along with overall Domain scores for the remaining Modules (Attention, Language, Spatial, and Executive Functions), were entered into a discriminant function analysis to evaluate the ability of each construct score or Domain score to predict group membership.

Hypothesis one: It was hypothesized that the Verbal Memory and Nonverbal Memory construct scores, along with the Language Domain score, would be more useful at predicting

group membership than other Domain scores individually. In particular, it was hypothesized that the Verbal Memory construct score derived from the NAB would be able to correctly predict group membership at a rate greater than chance in the current sample.

Hypothesis two: The Nonverbal Memory construct score derived from the NAB appears to have some significant limitations, especially when compared to the Nonverbal Memory construct score calculated in the Moser et al. (2000) study. Unlike the Moser study, whose Nonverbal Memory construct score was comprised of multiple spatial delayed recall tasks, the NAB Nonverbal Memory construct score has only one score, and, though clearly a test of spatial memory, is a recognition task rather than a spontaneous recall task. As recognition tasks are traditionally less difficult than recall tasks, and less specifically hippocampal-dependent because of the contribution of familiarity to recognition performance, scores in this Domain may be a less sensitive predictor of laterality unless the patient does extremely poorly. Therefore, it was predicted that the Nonverbal Memory construct score derived from the NAB would by itself be unable to correctly classify individuals in the current sample at a rate greater than chance.

After the discriminant function analysis was conducted, a multiple regression was also conducted to examine the overall amount of variance accounted for by the NAB Modules in regards to laterality in order to give a more general indication of the utility of the NAB in making a laterality determination in this population.

Question Two

The second question related solely to localization of seizure focus, another important factor in determining candidacy for epilepsy surgery. For this question, our primary focus was on patterned discrepancies in performance among different NAB Modules. Four performance discrepancy scores were calculated for each patient: Memory-Language discrepancy, Memory-Executive Functions discrepancy, Memory-Attention discrepancy, and Memory-Spatial

discrepancy. It was hypothesized that these discrepancy scores would be useful in clinical judgment as to whether the patients' seizures had a temporal vs. extratemporal focus. In this study, extratemporal classification included all seizure onsets occurring outside of the temporal lobe, including occipital, parietal, and frontal lobe foci, though the authors are aware that these seizure foci would likely present with very different patterns of neuropsychological performance. The aforementioned discrepancy scores, along with the individual Module scores by themselves (not calculated as discrepancies between Modules) were entered into a discriminant function analyses to determine 1) which methods provided better model fit and 2) how well they predicted temporal vs. extratemporal group membership based on final clinical judgment of seizure focus made by the comprehensive epilepsy program (CEP) team. This judgment took into account all available data, including video EEG, MRI and neuropsychological testing using a standard battery protocol.

Hypothesis three: It was hypothesized that the Memory-Spatial discrepancy score would provide the best prediction of group membership in regards to localization, as scores on the Memory, Attention, Language, and Executive Functions Modules are more likely to be positively correlated since all are in varying ways related to frontal lobe functioning; therefore, Memory-Attention, Memory-Executive Function, and Memory-Language discrepancy scores were hypothesized to be less predictive than Memory-Spatial discrepancy scores.

Table 1-1. Domains and Subtests of the Neuropsychological Assessment Battery (NAB)

Test*	Description
Screening-Orientation	Questions about orientation to self, time, place, and situation
Screening-Digits Forward	Repetition of orally presented digits
Screening-Digits Backward	Repetition of orally presented digits
Screening-Numbers & Letters	Two timed tasks (parts A & B) involving letter cancellation and letter cancellation plus serial addition, respectively
Screening-Auditory Comprehension	Three-part test that requires the examinee to demonstrate comprehension of orally presented commands
Screening-Naming	Visual confrontation naming task in which the examinee state the name of an object depicted in a photograph; semantic and phonemic cues are provided if necessary
Screening-Shape Learning	Single trial visual learning task involving multiple choice immediate recognition recall of five visual stimuli, followed by a delayed recognition task
Screening-Story Learning	Verbal learning task involving immediate and delayed free recall of a two sentence story
Screening-Visual Discrimination	Visual match-to-target paradigm, in which the examinee matches a target visual design from an array of four similar designs presented beneath the target
Screening-Design Construction	Visuoconstruction assembly task using plastic manipulatives (tans) to copy two-dimensional target designs (tangrams)
Screening-Mazes	Three timed paper-and-pencil mazes of increasing difficulty
Screening-Word Generation	Timed task in which the examinee creates three letter words from a group of six letters (two vowels, four consonants) that are presented visually
Attention-Orientation	Questions about orientation to self, time, place, and situation
Attention-Digits Forward	Repetition of orally presented digits
Attention-Digits Backward	Repetition of orally presented digits
Attention-Dots	Delayed recognition span paradigm, in which an array of dots is exposed for a brief period, followed by a blank interference page, followed by a new array with one additional dot; examinee points to new dot
Attention-Numbers and Letters	Four timed tasks (Parts A, B, C, and D) involving letter cancellation, letter counting, serial addition, and letter cancellation plus serial addition, respectively
Attention- Driving Scenes	Daily living task in which the examinee is first presented with a drawing of a driving scene as viewed from behind a steering wheel, and then shown another scene and asked to say and point to everything that is new, different, or missing relative to the previous scene; this is continued for four additional scenes
Language-Oral Production	Speech output task in which the examinee orally describes a picture of a family scene
Language-Auditory Comprehension	Six-part test that requires the examinee to demonstrate comprehension of orally presented instructions; tasks include performing one to four-step commands, the concepts of before/after, above/below, and right/left, body part identification, and paper folding

*Table information obtained from Chapter 1 (pages 6-10) of the Neuropsychological Assessment Battery: Administration, Scoring and Interpretation Manual (Stern & White, 2003).

Table 1-1. Continued

Test	Description
Language-Naming	Visual confrontation naming task in which the examinee states the name of a pictured object; semantic and phonemic cues are provided if necessary
Language-Reading Comprehension	Two-part test that requires the examinee to demonstrate reading comprehension of single words and of sentences by pointing to multiple choice written words and sentences that match visual stimuli
Language-Writing	Narrative writing task in which the examinee is shown the same drawing of a family scene used in the Oral Production test and asked to write about it; the writing sample is scored with regard to legibility, syntax, spelling, and conveyance
Language-Bill Payment	Daily living task in which the examinee is given a utility bill statement, check ledger, check, and envelope, and asked to follow a series of eight commands requiring oral and written responses of increasing complexity
Memory-List Learning	Verbal learning task involving three trials of a 12-word list, followed by an interference list, and then short-delay free recall, long-delay free recall, and long-delay forced-choice recognition tasks; the word list includes three embedded semantic categories with four words in each category
Memory- Shape Learning	Visual learning task involving three learning trials and multiple choice immediate recognition of nine visual stimuli, followed by delayed recognition and forced-choice recall
Memory-Story Learning	Verbal learning task involving immediate and delayed free recall of a five-sentence story; two learning trials are provided, and recall is scored for both verbatim and gist elements
Memory-Daily Living Memory	Verbal learning task involving three-trial learning with immediate recall, delayed recall, and delayed multiple-choice recognition of information encountered in daily living, including medication instructions, and a name, address, and phone number
Spatial-Visual Discrimination	Visual match-to-target paradigm, in which the examinee matches a target visual design from an array of four similar designs presented beneath the target
Spatial-Design Construction	Visuoconstruction assembly task using plastic manipulatives (tans) to copy two-dimensional target designs (tangrams)
Spatial-Figure Drawing	Visuoconstruction drawing task involving a copy and immediate recall of geometric figure of moderate complexity; the production is scored for the presence, accuracy, and placement of the elements, as well as overall organizational skill
Spatial-Map Reading	Daily living task in which the examinee answers questions (presented both orally and in writing) about a city map that has a compass rose and mileage legend
Executive Functions-Mazes	Seven timed paper and pencil mazes of increasing difficulty
Executive Functions-Judgment	Daily living test in which the examinee answers 10 judgment questions pertaining to home safety, health, and medical issues
Executive Functions-Categories	Classification and categorization task in which the examinee generates two-group categories based on photographs and verbal information about six people
Executive Functions-Word Generation	Timed task in which the examinee creates three-letter words from a group of eight letters (two vowels, six consonants) that are presented visually

Table 1-2. Test Composition of the UF Standard Neuropsychological Battery (SNB)

Test	Description
Wechsler Abbreviated Scale of Intelligence (WASI; Psychological Corporation, 1999)	Block Design, Matrix Reasoning, Vocabulary, and Similarities subtests adapted from Wechsler Scales of Intelligence
Rey Complex Figure Test and Recognition Trial (Myers & Myers, 2004)	Figural memory; Measure of visuoconstructive ability that incorporates immediate and delay recall.
California Verbal Learning Test- 2nd Edition (Delis et al., 2000)	Verbal memory test that assesses learning strategy, immediate and delayed recall, recognition, interference, and errors.
Wechsler Memory Scale-R; Logical Memory I, II; Visual Reproduction, I, II; Wechsler, 1987)	Measure of verbal and figure/nonverbal memory, respectively
Controlled Oral Word Association (COWA; Spreen & Benton, 1977)	Verbal fluency to alphabet letter (e.g., C,F,L).
Category Fluency – Animals (Tombaugh et al., 1999)	Verbal fluency to a semantic category in four 15” quarters.
Boston Naming Test- 2nd Edition (Goodglass & Kaplan, 2000)	Confrontation naming using large ink drawings
WASI Block Design subtest (Wechsler, 1997)	Visuoconstruction measure requiring reproduction of 2-dimensional designs with blocks
Wisconsin Card Sorting Test (Heaton, 1981)	Participants sort the cards based on their own principle. Measure of mental flexibility and problem solving
Trail Making Test (Reitan, 1958)	Visuomotor speed, tracking and attention between randomly placed numbers and letters
WAIS-III Digit Span (Wechsler, 1997)	Requires sustained attention and span
Finger Tapping (Halstead, 1947; Reitan & Wolfson, 1993)	Speeded gross motor movement
Grooved Pegboard Test (Klove, 1963)	Speeded fine motor movement
State Trait Anxiety Inventory (STAI; Spielberger, 1968)	40-item self-evaluation questionnaire assessing state and trait anxiety
Beck Depression Inventory-II (Beck, Steer, & Brown, 1996)	21-item questionnaire assessing elements of depression

CHAPTER TWO METHODS

Participants

Forty-five¹ individuals with documented or suspected epilepsy were recruited over a 16-month period from the comprehensive epilepsy program (CEP) at Shands at the University of Florida in Gainesville, Florida. The CEP inpatient unit admits, on average, 2.7 new inpatients per week for noninvasive (Phase I) video encephalographic (V-EEG) monitoring, and this admission rate was relatively consistent throughout the data collection phase of our study. All participants were identified, recruited and assessed during their Inpatient Phase I hospital stay in the epilepsy monitoring unit (EMU). Participants were included if they were 18 years of age or older, had documented or suspected epilepsy (from history and/or prior neurodiagnostic tests), were capable of undergoing neuropsychological testing and were willing to participate. Participants were excluded if they suffered from severe developmental disability or mental retardation resulting in IQ < 70 or an inability to participate, severe visual or auditory sensory deficits, history of Axis I psychiatric disturbance sufficiently significant to have resulted in hospitalization, or a current or past diagnosis of substance abuse or substance dependence². In addition, participants who experienced no electrographic events or definitive psychogenic non-epileptic seizures (PNES) during phase I monitoring were excluded from discriminant function analyses (DFA) and multiple regression analyses as the necessary calculation of the seizure lateralization index (SLI) would be unable to be determined for these individuals.

¹ This number was derived by estimating the minimum number of subjects per variable (5 to 7) required to provide adequate model stability during Discriminant Function Analyses.

² Due to patient confidentiality requirements, treating neurologists performed initial pre-screenings for recruitment. Precise numbers are unavailable for how many potential participants were eliminated by the neurologists prior to evaluating patient suitability for participation based on exclusionary criteria.

Of the 45 participants, gender composition was somewhat unbalanced, with 73% ($n = 33$) female participants compared to 27% ($n = 12$) male participants. Participants ranged in age from 21 to 66 years ($M = 43.16$, $SD = 12.24$). Education level ranged from 9 to 18 years ($M = 13.36$, $SD = 2.24$). The sample was 78% Caucasian ($n = 35$), 16% African American ($n = 7$), 2% Latino ($n = 1$), and 4% Native American ($n = 2$), a sample relatively in line with the Caucasian and African American demographics of the County and State in which the study took place, though the percentage of Latino participants was lower than expected. Approximately 93% of participants in the study ($n = 42$) identified themselves as being right-handed, whereas approximately 7% of participants ($n = 3$) identified themselves as left-handed. Sixty percent of participants in the study ($n = 27$) were administered the Form 1 version of the Neuropsychological Assessment Battery (NAB), while 40% of participants ($n = 18$) were administered the Form 2 version. Of the 45 participants in the study, 20 participants (44.4%) experienced clinical events during their inpatient stay that were in fact associated with genuine epileptic activity. Twelve participants (26%) experienced clinical events during their inpatient stay which, upon review, involved no epileptiform activity and were of sufficient type and quality to be confidently diagnosed by the attending neurologist post-discharge as psychogenic non-epileptic seizures (PNES). Finally, 13 participants (29%) who completed all testing for inclusion in our study, and who were subjected to multiple common triggers for seizure activity (e.g., sleep deprivation, exercise) nonetheless had no clinical events during their inpatient stay and, as a result, their seizures were not definitively diagnosed/localized.

Previous demographic information data was available for comparison from an existing database of 362 patients participating in this program. Unlike our study, the database contained a relatively comparable number of men and women (Male $n=173$; Female $n=179$). Caucasians

made up approximately 88.4% of patients in the database (n= 320), with African Americans (n=21, 5.8%), Hispanics (n=18, 5%), Asians (n=1, 0.3%), and “Other” (n=2; 0.6%) comprising the remainder of the sample. Mean level of education was approximately high school/general equivalency diploma (GED) range (12 years), with a standard deviation of 2.4 years (minimum = one year education; maximum = 21 years education).

Procedure

Participants were given the full NAB during their admission to the inpatient epilepsy monitoring unit (EMU) at Shands Hospital. All individuals participating in the comprehensive epilepsy program (CEP) at the University of Florida undergo MRI and Phase I monitoring, and many also undergo neuropsychological testing with the UF standard neuropsychological battery (SNB) as part of their diagnostic workup if they are considered to be a potential surgery candidate. The magnetic resonance imaging (MRI) results are analyzed by a board-certified neuroradiologist who provides diagnostic consultation to the CEP team. The electroencephalographic (EEG) findings are analyzed by a team of board-certified neurologists and epileptologists to determine localization of onset and seizure type. The SNB is supervised by licensed or board-certified neuropsychologists. Once all data are collected, the interdisciplinary CEP team meets to make a clinical judgment based on all available data in order to attempt to localize/lateralize seizure onset and select an appropriate mode of treatment. The average time of administration per participant was approximately 4 hours. Each participant was tested while in his or her room on the EMU. To control for variations in NAB administration, only the principal investigator and three trained research assistants tested participants. Besides the Screening Module, which was always administered first (as is standard), the remaining five Modules were administered to each participant in random order to minimize the likelihood of practice or order effects.

Statistical Analyses

Classification with Neuropsychological Tests

In surgical epilepsy centers, the results of the presurgical neuropsychological battery are used to predict lateralization and localization of seizures for purposes of surgical planning. Regarding lateralization, two neuropsychological patterns appear to be most critical. First, discrepancies between verbal and nonverbal memory are commonly seen in unilateral temporal lobe cases, particularly those involving seizure onsets in the language dominant temporal lobe where verbal memory is selectively impaired. Second, discrepancies between language and spatial functions are seen in unilateral cases, with language being most affected in left-onset epilepsy and spatial ability being most affected with onsets in the right hemisphere.

Seizure Lateralization Index (SLI)

To perform these analyses, we first classified patients as having left lateralized epilepsy, right lateralized epilepsy, or nonlateralized epilepsy/PNES and as having seizure foci in the temporal or “extratemporal” regions based on EEG data (in the case of EEG, the seizure lateralization index [SLI], adapted from Moser et al. (2000), was calculated in order to estimate the degree to which a person’s seizures were lateralized). The index, displayed in Equation 2-1:

$$\frac{(R-L)-0.5N}{R+L+N} \quad (2-1)$$

is calculated by determining the total number of right lateralized (labeled in Equation 2-1 as R), left lateralized (labeled in the Equation 2-1 as L), and nonlateralized (labeled in Equation 2-1 as N) seizures occurring while undergoing EEG monitoring. The numerator of this equation represents the degree to which seizures are lateralized to the right (positive values) or left (negative values) by first calculating a lateralization index $(R-L-0.5N)$. The number of nonlateralized seizures (N) is given a weight of 0.5 in the equation, as these seizures would have an equal chance of actually originating in either hemisphere, and are generally less definitive in

prediction than seizures with a clear hemispheric lateralization. The $(R-L/|R-L|)$ term in the numerator determines the arithmetic sign as positive or negative. The resulting index is then divided by the total number of electrographic events $(R+L+N)$, yielding a SLI that varies from -1 to +1. SLI values nearing -1.00 suggest seizure events lateralized entirely to the left hemisphere, whereas values nearing 1.00 suggest seizure events lateralized entirely to the right hemisphere. Values close to 0.00 suggest nonlateralized epilepsy (Moser, 2000). In this way, a patient who has six left lateralized seizures, no right lateralized seizures, and no nonlateralized seizures will obtain an SLI value of -1, a theoretically perfect prediction of left lateralization according to this equation. Conversely, a patient who has 12 left lateralized seizures, six right lateralized seizures, and no nonlateralized seizures, would obtain an SLI value of -0.5. Without appropriate weighting that considers the total number of seizures occurring, these two patients would have the same SLI value, even though they present with two very different clinical presentations based on this data (Moser, 2000). Participants who underwent 24-hour video EEG monitoring and were later determined to have PNES were given an SLI value of 0.00 in order to be included in quantitative analyses. The SLI was used as the primary criterion to address Question one. As stated previously, the 13 participants who experienced no electrographic events or definitive PNES during phase I monitoring were excluded from discriminant function and multiple regression analyses as the necessary calculation of the seizure lateralization index (SLI) could not be calculated for these individuals.

Exploratory and Advanced Analyses

After the SLI was calculated and each participants' NAB test scores (and NAB-derived scores specific to our study including the Verbal Memory construct score, Nonverbal Memory construct score, and four NAB Module discrepancy scores) were obtained along with their overall EMU findings regarding seizure localization, initial analyses were conducted to examine

the data including frequencies, descriptives, tests for normality, test for group differences, and correlations between variables.

In order to test hypotheses relating to the NAB's ability to predict seizure lateralization, separate discriminant function analyses were run using SLI as the outcome variable and (a) the Verbal Memory construct score as the sole predictor of lateralization, (b) the Nonverbal Memory construct score as the sole predictor of lateralization, and (c) the Verbal Memory and Nonverbal Memory construct scores together in combination with the four remaining full NAB Module scores [Attention, Language, Spatial, and Executive Functions] as predictor variables. The five Screening Module Domain scores in combination as predictor variables were also examined, though no a priori hypotheses were made with regard to their ability to predict lateralization. Two follow-up multiple regression analyses were then run using the SLI as the outcome variable. In the first analysis, the Verbal Memory and Nonverbal Memory construct scores were used as predictor variables. In the second, the five NAB Core Module scores (Attention, Language, Memory, Spatial, Executive Functions) served as predictor variables to examine the overall amount of variance accounted for by the NAB Modules in predicting seizure laterality.

In order to test our third Hypothesis with regard to the NAB's ability to predict localization of seizure focus, discriminant function analyses were run for Question Two using all patients who displayed electrographic seizures (excluding participants who were classified as having PNES). These analyses were conducted with the rationale that, while reducing the overall sample size of the analysis, a more accurate picture of the NAB's ability to predict localization would result. With the PNES subjects removed, the goal was to use NAB data to predict membership in the temporal lobe ($n = 14$) vs. extratemporal ($n = 6$) groups. Separate analyses were run using localization status (temporal vs. extratemporal) as the outcome variable, and (a)

the Memory-Attention discrepancy score as the sole predictor of localization, (b) the Memory-Language discrepancy score as the sole predictor, (c) the Memory-Spatial discrepancy score as the sole predictor, (d) the Memory-Executive Functions discrepancy score as the sole predictor, (e) these four NAB-derived discrepancy scores in combination as predictor variables and (f) the five Core NAB Module scores (Attention, Language, Memory, Spatial, Executive Functions) in combination as predictor variables. Since data were available, additional analyses were conducted using (a) the Verbal Memory construct score as the sole predictor, (b) the Nonverbal Memory construct score as the sole predictor, and (c) the five Screening Module Domain scores in combination as predictor variables. As above, no a priori hypotheses were made with regard to the ability of these variables to predict seizure localization to the temporal lobe. Stepwise DFAs were also run when variables were used in combination and at least one variable was statistically significant. In all discriminant function analyses in our study, only cross-validated grouped classification results were reviewed in order to increase overall generalizability to epilepsy populations as a whole.

CHAPTER THREE RESULTS

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) 18.0 software package. A minimum significance level of $p < .05$ was used throughout the analyses.

Normality and Group Differences on the Neuropsychological Assessment Battery

For ease of table reading, a variable name key was created and is displayed in Table 3-1. Descriptive statistics, including mean scores, standard deviations, and one-way analysis of variance (ANOVA) results by group based on epilepsy monitoring unit (EMU) findings (electrographic seizures, psychogenic non-epileptic seizures [PNES], no events) on all key Neuropsychological Assessment Battery (NAB) variables for our study are included in Table 3-2. Seizure lateralization index (SLI) distribution in participants experiencing electrographic seizures are included in Figure 3-1 (note: both subjects shown in Figure 3-1 with an SLI value of 0.33 had two seizures which localized to the right temporal lobe and one seizure which localized to the left temporal lobe. As both of these subjects were ultimately diagnosed with bitemporal lobe epilepsy and not considered to be potential candidates for seizure surgery, they were subsequently classified in our nonlateralized group during laterality-based analyses).

As can be seen from Table 3-2, NAB scores obtained from the sample in the present study were positively skewed, meaning the mean z-score obtained for each NAB-specific variable in the study was lower than the average z-score obtained from the NAB's standardization sample. Because of this, normality was examined using the Kolmogorov-Smirnov statistic (Corder & Foreman, 2009), which examines goodness of fit between the observed distribution and the normal distribution. With the exception of the Nonverbal Memory construct score ($p < .01$), all variables fit normality ($p > .05$). Because of this, subsequent analyses regarding group differences and the Nonverbal Memory construct score were conducted using independent

samples Mann-Whitney U tests (none of these tests showed significant group differences on any variables in our study with respect to the Nonverbal Memory construct score). For all other variables, normality was assumed and one-way ANOVAs with follow-up independent samples t-tests were run.

Group Differences by Demographics

No significant group differences ($p > .05$) were found on any NAB test Domain variables with regard to gender or handedness. An unexpected group difference was found with regard to form, such that the 27 participants in the study who were tested with Form 1 of the NAB had a lower Language Module Mean Domain score ($z = -.86$, $s.d. = 1.34$) than did the 18 participants who were tested with Form 2 of the NAB ($z = .01$, $s.d. = 1.44$) with a $t(43) = -2.07$, $p = .045$. This is an unusual finding and may potentially be explained by error variance given our small sample as there is no significantly plausible reason why this group difference would have occurred (both forms were given in alternating fashion to participants, and all trained test administrators utilized both forms). Psychometric data included in Chapter 5 of the NAB Psychometric and Technical Manual (White & Stern, 2003) showed that tests of equivalent forms reliability between Form 1 and Form 2 of the NAB Language Module using generalizability theory produced a generalizability (G) coefficient of .62. According to Cicchetti & Sparrow (1981), generalizability coefficients of .60 or higher are regarded as demonstrating very good reliability.

Group Differences by EMU Classification

When comparing the individuals in our study who had electrographic seizures ($n = 20$) to those who were classified as having psychogenic NES ($n = 12$) vs. those who experienced no clinical events during one-way ANOVAs, no statistically significant group differences in any NAB variable were found.

Group Differences by Lateralization Classification

When comparing groups based on lateralization classification (left lateralized seizures [n = 4] vs. right lateralized seizures [n = 11] vs. nonlateralized seizures/PNES [n = 17]), a statistically significant group difference ($F [2, 29] = 3.73, p < .05$) was found on the Memory-Spatial discrepancy score during one-way ANOVAs. Subsequent t-tests revealed statistically significant group differences between the left lateralized and right lateralized groups ($t [13] = -3.24, p < .01$) as well as the left lateralized and nonlateralized groups ($t [19] = -2.22, p < .05$), while tests of group differences between the right lateralized and nonlateralized groups were nonsignificant ($t [26] = .396, p > .05$). Individuals in the left lateralized group had a mean z-score on this NAB-derived variable over one standard deviation (Mean $z = -1.76, s.d. = 0.93$) lower than individuals in the right lateralized (Mean $z = -0.45, s.d. = 0.60$) or nonlateralized (Mean $z = -0.58, s.d. = 0.96$) groups. Further explication of this group difference is discussed in the Correlations section.

Group Differences by Localization Classification

With regards to individuals in the study who were classified as having temporal lobe epilepsy (n = 14) vs. those classified as having seizures of “extratemporal” focus (n = 6), group differences were found on the Screening-Spatial Domain score ($t [18] = -2.25, p < .05$), Screening-Executive Functions Domain score ($t [18] = -2.47, p < .05$), Attention Module score ($t [18] = -2.31, p < .05$), Memory-Attention discrepancy score ($t [18] = -2.38, p < .05$), and Verbal Memory construct scores ($t [18] = -4.30, p < .001$). Individuals with temporal lobe epilepsy performed approximately one standard deviation or more below individuals having seizures of extratemporal focus on all five of these variables. T test values and associated significance levels for each of these variables are also displayed in Table 3-5.

Correlations

Bivariate correlations were conducted to further explore relationships between variables. Positive correlations between education and all NAB-derived scores (excluding the discrepancy scores) were found. Nearly all of these scores were in fact statistically significant at the $p < .05$ level, with the exceptions of the NAB Total Score, Attention Module score, and Language Module score. All NAB-derived scores (again, excluding the discrepancy scores) were positively correlated with each other ($p < .001$). Notably, we observed a positive correlation of SLI score with Memory-Spatial discrepancy score (Pearson's $r = .376$, $p < .05$), suggesting that as the Memory-Spatial discrepancy score increased (suggesting more intact memory than spatial ability), the SLI value also increased (towards a value of 1.0, which represents a strongly right lateralized seizure focus). This correlation suggests that individuals with a higher Memory-Spatial discrepancy score were associated with more right lateralized seizures, a correlation that provides some support for the utility of the NAB in predicting seizure lateralization.

Question One

Discriminant Function Analyses

Descriptive statistics (including means, standard deviations and one-way ANOVAs) for groups by lateralization classification (left lateralized seizures, right lateralized seizures, and nonlateralizing seizures/PNES) are included in Table 3-3. The classification rates for each predictor variable in our hypotheses, including percentage correct classification and information regarding base rates of occurrence for each lateralization subset, are included in Table 3-4.

As can be seen in Table 3-4, no variables or combinations of variables in our study were able to correctly classify individuals by lateralization at a rate greater than chance given the base rates of occurrence in our study. Therefore, the hypothesis that the Verbal Memory construct

score derived from the NAB would be able to correctly predict lateralization at a rate greater than chance was not supported. Our second Hypothesis (that the Nonverbal Memory construct score derived from the NAB would be unable to predict lateralization at a rate greater than chance) was not disconfirmed. Stepwise DFAs were not conducted for these lateralization-based analyses since no predictor variables reached statistical significance. Even the Memory-Spatial discrepancy score, the only variable in our study which was significantly correlated with SLI value (Pearson's $r = .376$, $p = .034$) was unable to classify individuals based on lateralization at a rate greater than chance.

The following is a description of each set of predictors used in these discriminant analyses, the resulting Wilks λ values, and levels of statistical significance. Entering the Verbal Memory construct score as the sole predictor of lateralization yielded the following results: Wilks $\lambda = 0.949$ ($p = .47$), $n = 32$; the Nonverbal Memory construct score as the sole predictor: Wilks $\lambda = .985$ ($p = .80$), $n = 32$; The two Memory-derived construct scores in combination with the four remaining NAB Module scores (Attention, Language, Spatial, Executive Functions) as predictors: Wilks $\lambda = .542$ ($p = .18$), $n = 32$; The five Screening Module Domain scores in combination as predictors: Wilks $\lambda = .791$ ($p = .79$), $n = 32$.

Similar discriminant function analyses were run for Question One excluding participants who were classified as having NES, causing the groups to be: left lateralized $n = 4$, right lateralized $n = 11$, nonlateralized $n = 5$. None of these analyses yielded statistically significant results, and none were able to achieve greater-than-chance correct classification into laterality groups based on participant NAB scores.

Multiple Regression Analyses

Multiple regressions were conducted to examine the overall amount of variance accounted for by the NAB Modules in regards to laterality in order to give a more general indication of the utility of the NAB with this particular patient population. A multiple regression using the Verbal Memory and Nonverbal Memory construct scores as predictor variables was nonsignificant ($F[29] = .570$, $p = .572$, adjusted $R^2 = .029$). A second multiple regression using the five Core NAB Modules (Attention, Language, Memory, Spatial, Executive Functions) as predictor variables, while appearing to be a better overall model, was also nonsignificant ($F[26] = 1.846$, $p = .139$, adjusted $R^2 = .120$). The small n available for inclusion ($n = 32$) likely reduced the overall stability of these regression analyses.

Question Two

Descriptive statistics (including means, standard deviations, and independent samples t -tests) by localization classification excluding participants with PNES are included in Table 3-5. The classification rates for each predictor variable in our hypotheses, including percentage correct classification and information regarding base rates of occurrence for each localization subset when PNES patients were excluded from the analysis are included in Table 3-6.

Unlike lateralization prediction, some variables in our study were able to predict seizure localization at a rate greater than chance. Five variables predicted localization at statistically significant levels, including the Screening-Spatial Domain score (Pearson's $r = .469$, $p = .037$), Screening-Executive Functions Domain score (Pearson's $r = .504$, $p = .024$), Attention Module score (Pearson's $r = .479$, $p = .033$), and Memory-Attention discrepancy score (Pearson's $r = .489$, $p = .029$). Lastly, the Verbal Memory construct score, which was derived primarily to evaluate lateralization in our analyses (and which did a poor job at doing so), turned out to be highly correlated with localization of seizure focus (Pearson's $r = .712$, $p < .001$), such that

higher (better) Verbal Memory construct scores were associated with membership in the extratemporal seizure focus group.

In DFA analyses, the Memory-Attention discrepancy score by itself was able to correctly classify 92.9% of temporal lobe cases, but was able to classify cases with extratemporal seizure focus with only 50% accuracy. Even with PNES subjects excluded, the other three discrepancy scores (Memory-Language discrepancy, Memory-Spatial discrepancy, and Memory-Executive Functions discrepancy) were unable to adequately classify individuals based on group membership. Using all four discrepancy score variables in combination in a stepwise DFA provided no greater classification accuracy than using the Memory-Attention discrepancy score alone. Using the 5 core NAB Modules (Attention, Language, Memory, Spatial, Executive Functions) in combination in a stepwise DFA, temporal seizure focus was predicted at a rate slightly greater than chance (85.7%). However, this combination of variables was able to predict extratemporal seizure focus with only 50% accuracy. Similar findings were found when using the 5 Screening Modules Domain scores (Screening-Attention, Screening-Language, Screening-Memory, Screening-Spatial, Screening-Executive Functions) in combination, as this stepwise DFA was able to correctly classify 92.9% (13/14) of the cases with temporal lobe seizures, but only 50% (3/6) of the cases whose seizures were of extratemporal focus.

The Verbal Memory construct score, while originally intended to examine lateralization rather than localization of seizure focus, appeared to exhibit the best predictive ability of any variable in our entire study. As the sole predictor of seizure localization in individuals with known seizures, the Verbal Memory construct score correctly classified 90% of cases correctly grouping 92.9% (13/14) of the participants with temporal lobe seizure focus and 83.3% (5/6) of the participants with extratemporal seizures.

Despite our predictions that the NAB-derived discrepancy scores (Memory-Attention discrepancy, Memory-Language discrepancy, Memory-Spatial discrepancy, and Memory-Executive Functions discrepancy) would be particularly useful in predicting localization, only the Memory-Attention discrepancy score was able to predict localization at a rate greater than chance. As such, our third Hypothesis (that the Memory-Spatial discrepancy score would provide the best prediction of group membership in regards to localization) was not supported.

The following is a description of each set of predictors used in these discriminant analyses, the resulting Wilks λ values, and levels of statistical significance. Entering the Memory-Attention discrepancy score as the sole predictor of localization when PNES participants were excluded yielded the following results: Wilks $\lambda = .761$ ($p = .029$), $n = 20$; the Memory-Language discrepancy score as the sole predictor: Wilks $\lambda = .997$ ($p = .80$), $n = 20$; the Memory-Spatial discrepancy score as the sole predictor: Wilks $\lambda = .999$ ($p = .90$), $n = 20$; the Memory-Executive Functions discrepancy score as the sole predictor: Wilks $\lambda = .955$ ($p = .37$), $n = 20$.

When the four NAB-derived discrepancy scores (Memory-Attention discrepancy, Memory-Language discrepancy, Memory-Spatial discrepancy, and Memory-Executive Functions discrepancy) were used in combination as predictors, the following results were obtained: Wilks $\lambda = .652$ ($p = .14$), $n = 20$; the four NAB-derived discrepancy scores (Memory-Attention discrepancy, Memory-Language discrepancy, Memory-Spatial discrepancy, and Memory-Executive Functions discrepancy) in combination as predictors in a stepwise DFA: Wilks $\lambda = .761$ ($p = .029$), $n = 20$. The Verbal Memory construct score as the sole predictor of localization yielded the following: Wilks $\lambda = 0.492$ ($p < .001$), $n = 20$, while the Nonverbal Memory construct score as the sole predictor produced a Wilks $\lambda = .836$ ($p = .076$), $n = 20$.

The five Core NAB Module scores (Attention, Language, Memory, Spatial, Executive Functions) used in combination as predictors of localization yielded the following: Wilks $\lambda = .672$ ($p = .29$), $n = 20$; the five Core NAB Module scores (Attention, Language, Memory, Spatial, Executive Functions) used in combination as predictors of localization in a stepwise analysis: Wilks $\lambda = .771$ ($p = .033$), $n = 20$. When the five NAB Screening Module Domain scores (Screening-Attention, Screening-Language, Screening-Memory, Screening-Spatial, and Screening-Executive Functions) were entered in combination as predictors of localization, the following results were obtained: Wilks $\lambda = .448$ ($p = .029$), $n = 20$; the five NAB Screening Module Domain scores (Screening-Attention, Screening-Language, Screening-Memory, Screening-Spatial, and Screening-Executive Functions) in combination as predictors of localization in a stepwise analysis: Wilks $\lambda = .746$ ($p = .024$), $n = 20$.

Table 3-1. Variable Name Key

Variable	Variable coding
Screening NAB Total Score	S-NAB
Screening Attention Domain score	S-ATT
Screening Language Domain score	S-LAN
Screening Memory Domain score	S-MEM
Screening Spatial Domain score	S-SPT
Screening Executive Functions Domain score	S-EXE
Full NAB Total score	NAB
Attention Module score	ATT
Language Module score	LAN
Memory Module score	MEM
Spatial Module score	SPT
Executive Functions Module score	EXE
Verbal Memory construct score	VMEM
Nonverbal Memory construct score	NVMEM
Memory-Attention discrepancy score	MEMATTDISC
Memory-Language discrepancy score	MEMLANDISC
Memory-Spatial discrepancy score	MEMSPTDISC
Memory-Executive Functions discrepancy score	MEMEXEDISC

Table 3-2. Descriptive Statistics by Seizure Classification/Epilepsy Monitoring Unit (EMU) Outcome

	Grand mean (SD) (N=45)	Electrographic seizures mean (SD) (N=20)	PNES mean (SD) (N=12)	No events mean (SD) (N=13)	One-way ANOVA*
Age	43.16 (12.24)	40.95 (12.97)	47.17 (9.13)	43.85 (13.51)	F (2,42) = 0.97
Education	13.36 (2.24)	13.15 (2.18)	13.50 (2.71)	13.54 (1.98)	F (2, 42) = 0.15
S-NAB	-1.21 (1.30)	-1.53 (1.16)	-1.25 (1.33)	-0.70 (1.43)	F (2, 42) = 1.63
S-ATT	-1.11 (1.33)	-1.18 (1.28)	-1.18 (1.39)	-0.94 (1.45)	F (2, 42) = 0.14
S-LAN	-1.60 (1.23)	-1.94 (1.10)	-1.52 (1.45)	-1.16 (1.14)	F (2, 42) = 1.70
S-MEM	-1.56 (1.27)	-1.76 (1.20)	-1.48 (1.47)	-1.34 (1.24)	F (2, 42) = 0.45
S-SPT	-0.70 (1.28)	-0.93 (1.39)	-0.60 (1.11)	-0.44 (1.29)	F (2, 42) = 0.64
S-EXE	-0.99 (1.24)	-0.88 (1.28)	-1.13 (1.28)	-1.03 (1.21)	F (2, 42) = 0.16
NAB	-0.78 (1.06)	-0.65 (1.02)	-1.12 (1.13)	-0.68 (1.10)	F (2, 42) = 0.80
ATT	-1.05 (1.26)	-1.02 (1.24)	-1.08 (1.18)	-1.06 (1.45)	F (2, 42) = 0.01
LAN	-0.52 (1.43)	-0.71 (1.02)	-0.60 (1.43)	-0.13 (1.93)	F (2, 42) = 0.66
MEM	-0.23 (1.59)	-0.14 (1.47)	-0.77 (1.52)	0.12 (1.83)	F (2, 42) = 1.03
SPT	-0.80 (1.28)	-1.18 (1.20)	-0.68 (1.27)	-0.33 (1.34)	F (2, 42) = 1.87
EXE	-0.91 (1.35)	-1.20 (1.30)	-0.54 (1.35)	-0.80 (1.43)	F (2, 42) = 0.97
VMEM	-0.34 (0.94)	-0.30 (1.03)	-0.55 (0.89)	-0.22 (0.88)	F (2, 42) = 0.41
NVMEM	0.02 (1.13)	0.20 (1.12)	-0.13 (1.32)	-0.11 (1.02)	F (2, 42) = 0.44
MEMATTDISC	0.52 (0.93)	0.74 (0.76)	0.40 (1.01)	0.28 (1.09)	F (2, 42) = 1.11
MEMLANDISC	-0.05 (0.80)	-0.14 (0.85)	0.05 (0.80)	-0.03 (0.80)	F (2, 42) = 0.21
MEMSPTDISC	-0.83 (1.08)	-0.90 (0.93)	-0.31 (0.83)	-1.18 (1.36)	F (2, 42) = 2.24
MEMEXEDISC	-0.14 (0.90)	0.18 (0.74)	-0.54 (0.72)	-0.26 (1.13)	F (2, 42) = 2.84

* F-ratios reaching significance at $p < .05$ are annotated by a *; $p < .01$, **; $p < .001$, ***

Table 3-3. Descriptive Statistics by Lateralization Classification

	All participants mean (SD) (N=32)	Left lateralized seizures mean (SD) (N=4)	Right lateralized seizures mean (SD) (N=11)	Nonlateralizin g seizures/PNES mean (SD) (N=17)	One-way ANOVA*
Age	43.28 (11.92)	46.75 (14.18)	42.55 (12.85)	42.94 (11.44)	F (2, 29) = 0.18
Education	13.28 (2.36)	14.25 (2.06)	12.91 (2.39)	13.29 (2.47)	F (2, 29) = 0.46
S-NAB	-1.42 (1.21)	-2.23 (0.25)	-1.21 (1.26)	-1.37 (1.28)	F (2, 29) = 1.10
S-ATT	-1.18 (1.30)	-1.98 (0.50)	-0.98 (1.28)	-1.13 (1.42)	F (2, 29) = 0.90
S-LAN	-1.79 (1.24)	-3.00 (0.51)	-1.60 (1.08)	-1.60 (1.34)	F (2, 29) = 2.38
S-MEM	-1.65 (1.30)	-2.77 (0.45)	-1.38 (1.27)	-1.57 (1.35)	F (2, 29) = 1.85
S-SPT	-0.80 (1.28)	-1.54 (0.94)	-0.66 (1.46)	-0.73 (1.24)	F (2, 29) = 0.74
S-EXE	-0.98 (1.26)	-1.47 (0.86)	-0.74 (1.35)	-1.01 (1.30)	F (2, 29) = 0.49
NAB	-0.82 (1.07)	-0.43 (0.64)	-0.32 (0.79)	-1.24 (1.16)	F (2, 29) = 3.21
ATT	-1.04 (1.20)	-1.84 (0.56)	-0.70 (1.16)	-1.08 (1.28)	F (2, 29) = 1.37
LAN	-0.67 (1.17)	-0.98 (0.26)	-0.85 (0.92)	-0.48 (1.43)	F (2, 29) = 0.48
MEM	-0.38 (1.50)	-0.08 (0.95)	-0.30 (1.00)	-0.50 (1.87)	F (2, 29) = 0.15
SPT	-1.00 (1.23)	-1.58 (0.76)	-0.83 (1.40)	-0.97 (1.22)	F (2, 29) = 0.54
EXE	-0.95 (1.34)	-2.23 (0.36)	-0.87 (1.32)	-0.71 (1.38)	F (2, 29) = 2.30
VMEM	-0.39 (0.98)	-0.90 (0.66)	-0.18 (0.93)	-0.41 (1.06)	F (2, 29) = 0.79
NVMEM	0.08 (1.19)	-0.10 (0.73)	0.27 (1.23)	-0.01 (1.28)	F (2, 29) = 0.23
MEMATTDISC	0.61 (0.86)	0.93 (0.88)	0.68 (0.64)	0.49 (1.00)	F (2, 29) = 0.46
MEMLANDISC	-0.07 (0.83)	-0.37 (1.02)	0.04 (0.90)	-0.06 (0.77)	F (2, 29) = 0.35
MEMSPTDISC	-0.68 (0.93)	-1.76 (0.93)	-0.45 (0.60)	-0.58 (0.96)	F (2, 29) = 3.73*
MEMEXEDISC	-0.09 (0.80)	0.40 (0.47)	0.17 (0.76)	-0.37 (0.81)	F (2, 29) = 2.55

* F-ratios reaching significance at $p < .05$ are annotated by a *, $p < .01$, **, $p < .001$, ***

Table 3-4. Percentage Correct Classification of Seizure Lateralization Using NAB Variables as Predictors

Predictor variables	Left lateralized seizures (n=4; 12.5% base rate of occurrence)	Right lateralized seizures (n = 11; 34.4% base rate of occurrence)	Nonlateralized seizures/PNES (n = 17; 53.1% base rate of occurrence)
VMEM	0.00% (0/4)	0.00% (0/11)	88.2% (15/17)
NVMEM	0.00% (0/4)	0.00% (0/11)	100% (17/17)
VMEM, NVMEM, ATT, LAN, SPT, EXE	50.0% (2/4)	18.2% (2/11)	70.6% (12/17)
S-ATT, S-LAN, S- MEM, S-SPT, S-EXE	0.00% (0/4)	0.00% (0/11)	58.8% (10/17)

Table 3-5. Descriptive Statistics by Localization Classification (Excluding Participants with Psychogenic Non-epileptic Seizures [PNES])

	All participants mean (SD) (N=20)	Temporal lobe seizure localization mean (SD) (N=14)	“Extratemporal” seizure localization mean (SD) (N=6)	Independent samples t-tests* (N = 20, df =18)
Age	40.95 (12.97)	43.86 (12.86)	34.17 (11.41)	1.60
Education	13.15 (2.18)	12.86 (2.41)	13.83 (1.47)	-0.91
S-NAB	-1.53 (1.16)	-1.77 (1.13)	-0.95 (1.08)	-1.52
S-ATT	-1.19 (1.28)	-1.54 (1.26)	-0.37 (0.98)	-2.02
S-LAN	-1.95 (1.11)	-2.13 (1.22)	-1.52 (0.71)	-1.13
S-MEM	-1.76 (1.20)	-1.90 (1.31)	-1.43 (0.92)	-0.79
S-SPT	-0.93 (1.39)	-1.35 (1.36)	0.03 (0.94)	-2.25*
S-EXE	-0.88 (1.28)	-1.30 (1.30)	0.08 (0.45)	-2.47*
NAB	-0.64 (1.02)	-0.70 (0.96)	-0.52 (1.22)	-0.35
ATT	-1.02 (1.24)	-1.40 (1.20)	-0.14 (0.87)	-2.31*
LAN	-0.71 (1.02)	-0.99 (0.94)	-0.05 (0.97)	-2.03
MEM	-0.14 (1.47)	-0.50 (1.33)	0.71 (1.52)	-1.80
SPT	-1.18 (1.20)	-1.24 (1.29)	-1.06 (1.05)	-0.30
EXE	-1.20 (1.31)	-1.48 (1.38)	-0.55 (0.93)	-1.50
VMEM	-0.30 (1.03)	-0.77 (0.75)	0.80 (0.73)	-4.30***
NVMEM	0.20 (1.12)	-0.09 (1.07)	0.87 (1.00)	-1.88
MEMATTDISC	0.74 (0.76)	0.51 (0.77)	1.30 (0.37)	-2.38*
MEMLANDISC	-0.14 (0.85)	-0.10 (0.94)	-0.21 (0.68)	0.25
MEMSPTDISC	-0.90 (0.93)	-0.89 (0.88)	-0.94 (1.11)	0.12
MEMEXEDISC	0.19 (0.74)	0.09 (0.78)	0.42 (0.65)	-.921

*Independent samples t-tests described in the rightmost column describe differences between temporal and extratemporal groups. T-tests reaching significance at $p < .05$ are annotated by a *; $p < .01$, **; $p < .001$, ***

Table 3-6. Percentage Correct Classification of Seizure Localization (Excluding Participants with PNES) Using NAB Variables as Predictors

Predictor variables	Temporal lobe seizure localization (n=14; 70% base rate of occurrence)	“Extratemporal” seizure localization (n=6; 30% base rate of occurrence)
MEMATTDISC	92.9% (13/14)	50.0% (3/6)
MEMLANDISC	100% (14/14)	0.00% (0/6)
MEMSPTDISC	100% (14/14)	0.00% (0/6)
MEMEXEDISC	92.9% (13/14)	0.00% (0/6)
MEMATTDISC, MEMLANDISC, MEMSPTDISC, MEMEXEDISC	85.7% (12/14)	33.3% (2/6)
MEMATTDISC, MEMLANDISC, MEMSPTDISC, MEMEXEDISC (stepwise)	92.9% (13/14)	50.0% (3/6)
VMEM	92.9% (13/14)	83.3% (5/6)
NVMEM	92.9% (13/14)	16.7% (1/6)
ATT, LAN, MEM, SPT, EXE	78.6% (11/14)	16.7% (1/6)
ATT, LAN, MEM, SPT, EXE (stepwise)	85.7% (12/14)	50.0% (3/6)
S-ATT, S-LAN, S-MEM, S-SPT, S-EXE	85.7% (12/14)	66.7% (4/6)
S-ATT, S-LAN, S-MEM, S-SPT, S-EXE (stepwise)	92.9% (13/14)	50.0% (3/6)

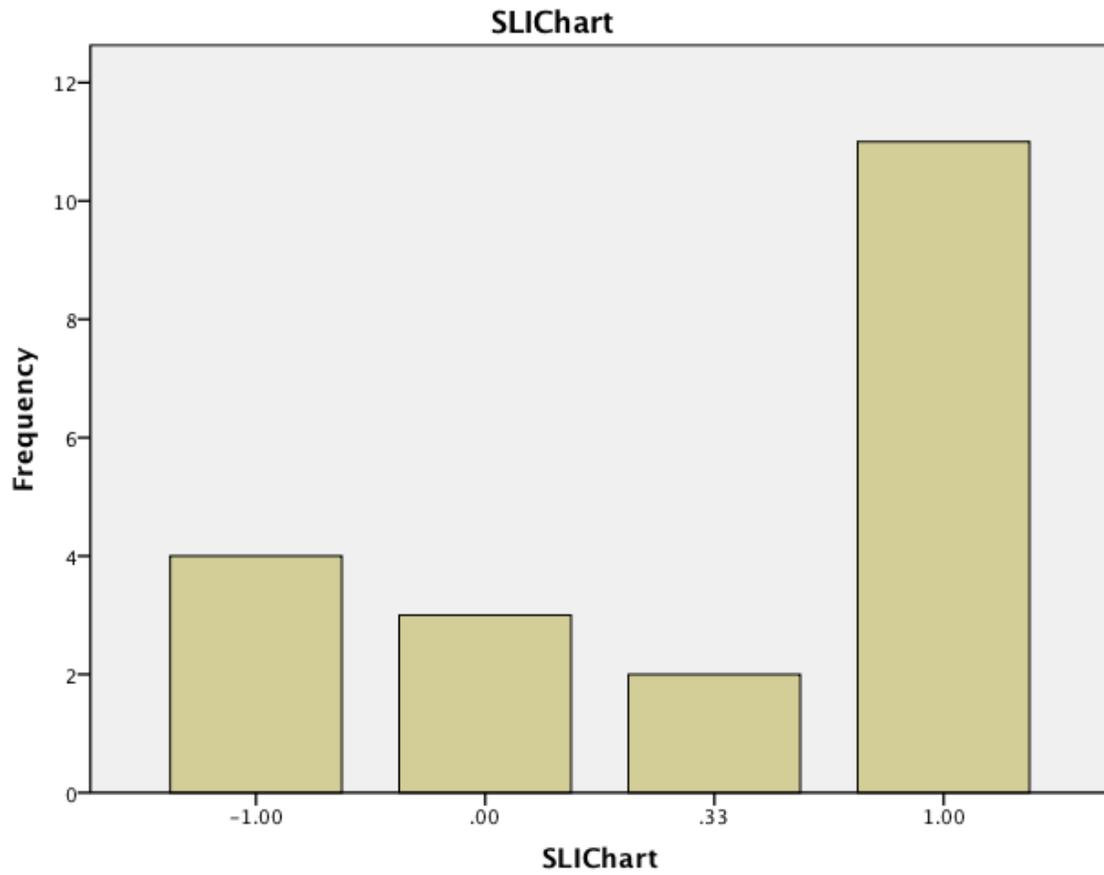


Figure 3-1. Seizure Lateralization Index (SLI) Distribution of Participants Experiencing Electrographic Seizures

CHAPTER FOUR DISCUSSION

Results Summary

This study attempted to assess the clinical utility of the Neuropsychological Assessment Battery (NAB) in an epilepsy population by analyzing how well NAB scores (as well as specific additional variables derived from NAB scores) predicted lateralization and localization of seizure focus in our sample. Over a 16-month data-collection period, 45 participants with documented or suspected epilepsy were tested while undergoing 24-hour video electroencephalographic (V-EEG) monitoring during their inpatient stay on the epilepsy monitoring unit (EMU) at UF/Shands Hospital in Gainesville, Florida. Each participant was administered the NAB Screening Module as well as the five Core NAB Modules (Attention, Language, Memory, Spatial, and Executive Functions). With the exception of the Screening Module, which was designed to be administered first, the remaining five NAB Modules were administered in random order to minimize practice or order effects. Both forms of the NAB were also used with alternating participants to attempt to increase generalizability. After testing was completed and NAB scores were obtained, additional NAB-derived scores were calculated for additional use in our analyses. Specifically, various subtest scores within the NAB Memory Modules were used to calculate Verbal Memory and Nonverbal Memory construct scores based on which inherent form of Memory ability these particular subtests assessed. These scores were primarily calculated in order to further assess the NAB's ability to predict lateralization of seizure focus in our sample.

It was hypothesized that the derived Verbal Memory construct score would be able to predict lateralization of seizure focus in our sample at a rate greater than chance during discriminant function analyses. As the NAB's Memory Module contains only one measure

assessing nonverbal memory abilities (NAB Shape Learning) and this measure is a recognition measure, which are in general less difficult than free recall measures (such as the List Learning and Story Learning subtests which derived the Verbal Memory construct score), it was also hypothesized that the Nonverbal Memory construct score by itself would be unable to predict lateralization during discriminant function analyses. With regard to prediction of localization of seizure focus, it was hypothesized that NAB-derived Module discrepancy scores (Memory-Attention discrepancy score, Memory-Language discrepancy score, Memory-Spatial discrepancy score, and Memory-Executive Functions discrepancy score) would be able to predict localization of seizure focus at a rate greater than chance within our sample, with the Memory-Spatial discrepancy score predicted to have the best ability to classify subjects as having seizures of temporal vs. extratemporal focus.

Of the 45 participants tested, twenty were found to have electrographic seizures (four left lateralized, eleven right lateralized, and five nonlateralized), twelve were found to have psychogenic non-epileptic seizures (PNES), and thirteen subjects had no clinical events during their stay and were therefore unable to be definitively diagnosed or classified. Despite data being positively skewed for our sample, tests of normality using Kolmogorov-Smirnov statistics for the variables in our study were nonsignificant ($p > .05$), with the exception of the Nonverbal Memory construct score ($p < .01$). As such, tests for group differences for this particular variable were assessed using nonparametric tests and all were nonsignificant). No group differences were found on key demographic variables including gender or handedness. A group difference was found on the Language Module score by which NAB Form was administered; however, this difference is likely due to error given our small sample size. No group differences were found on NAB scores with respect to EMU classification (electrographic seizures vs. PNES

vs. No events). With regard to lateralization classification (left lateralized seizures vs. right lateralized seizures vs. nonlateralized seizures/PNES), a statistically significant group difference was found on the Memory-Spatial discrepancy score, which lent some credence to our initial hypotheses regarding the potential utility of this score. With regard to localization classification (temporal lobe seizures vs. seizures originating outside the temporal lobe), statistically significant group differences were found on five separate NAB variables (Screening-Spatial Domain score, Screening-Executive Functions Domain score, Attention Module score, Memory-Attention discrepancy score, and the Verbal Memory construct score).

Discriminant function analyses (DFAs) showed an inability for the NAB scores and additional NAB-derived scores obtained in our study to predict lateralization at a rate greater than chance. Even the Memory-Spatial discrepancy score, the only variable in our study where group differences based on laterality were found, was unable to adequately predict group membership.

In contrast, a number of variables in our study (including the Memory-Attention discrepancy score, NAB Core Modules in combination, NAB Screening Modules in combination, and Verbal Memory discrepancy score) predicted localization of seizure focus at a rate greater than chance. The Verbal Memory construct score in particular was able to correctly classify individuals by localization with 90% accuracy, providing the strongest evidence in our study of the NAB's potential clinical utility with this population.

Study Limitations

The results of our study, along with the study itself, have several limitations that warrant acknowledging. The small sample size for our study likely reduced the robustness and power of some of our analyses (e.g., multiple regressions) to detect group differences (though the current scores obtained would not have been significant at the $p < .05$ level even if our sample included

over 1,000 participants). There were a number of unforeseen logistical challenges that made data collection with this specialized population more challenging than was originally anticipated, including enhanced privacy protections (which, while vital, presented as additional barriers to access), availability of trained research assistants, etc. In addition, data were collected on 45 participants, but only 20 (44%) actually experienced electrographic seizures, while 12 (27%) experienced PNES and 13 (29%) had no clinical events. While these outcome rates were confirmed by UF neurologists to be fairly consistent with average EMU outcomes, the return rate of participants experiencing electrographic seizures (44%) compared to participants experiencing other outcomes (56%) was substantially lower than anticipated at study outset.

Another potential limitation involves the high female-to-male (33:12) ratio of participants in our study. Previous data available for comparison from an existing database of 362 patients participating in this program contained a more comparable number of men and women (Male n=173; Female n=179). It is unknown why our rate of female to male participants differed so greatly. Research has shown that there are notable differences between men and women with epilepsy, including men being significantly more likely to experience generalized seizures than women (Janszky, Shulz, Janszky, & Ebner, 2004) while women are more likely to experience isolated auras and have lateralized electroencephalographic (EEG) seizure patterns more often than men (McHugh & Delanty, 2008). In addition, Frings et al. (2006) found that, during memory processing, hippocampal activation is significantly more left lateralized in healthy women and more right lateralized in healthy men (with women subsequently rating their strategies during memory testing as being more verbal than men in the same study). Limited information is currently available in the literature, however, with regard to gender differences on neurocognitive test performance specifically within epilepsy populations, and therefore the

extent to which this gender discrepancy may have impacted the results of the current study is unknown.

As our study was a single-site study, sampling participants from a limited geographical region of the Southeastern United States, it is unknown to what extent our results may generalize to epilepsy populations located in other regions of the United States or other countries.

Possible Reasons for Study Outcome

In addition to the small sample size mentioned previously, there was a notable size discrepancy based on lateralization outcome, such that only four participants were in the left lateralized group, while eleven participants were in the right lateralized group and seventeen participants were in the nonlateralized/PNES group (five participants with nonlateralized electrographic seizures and twelve participants diagnosed with PNES). These differences in group size, in conjunction with the initial small sample size and nonsignificant differences between group mean scores on NAB variables, caused many of our laterality-specific DFAs to perform poorly, even when follow-up analyses were run excluding participants with PNES. While it appears that the NAB genuinely possesses weaker sensitivity to right-temporal dysfunction due to reduced sampling of nonverbal as compared to verbal memory abilities (e.g., Shape Learning is purely recognition-based, thus reducing sensitivity of the Nonverbal Memory construct score), grossly unequal group sizes in the lateralization groups also likely reduced the NAB's performance as a laterality predictor.

With regard to the NAB's weaker sensitivity to right-temporal dysfunction, it is worth noting that the Shape Learning test in the NAB Memory Module, while being a purely recognition measure, is not the only nonverbal memory test in the NAB. The Figure Drawing test included in the Spatial Module of the NAB bears much similarity to the Rey Complex Figure Test (Myers & Myers, 2004). The test assesses visuoperceptual/visuoconstructional abilities by

requiring the individual being tested to reproduce a complex geometric figure with as much fidelity as possible. The Rey Complex Figure Test includes a copy, immediate recall, and delayed recall condition that occurs after 30 minutes (as well as an optional recognition task) which allows the ability to assess nonverbal memory abilities while simultaneously assessing the individuals' visuo-perceptual/visuo-constructional skills. During initial test development and standardization, the creators of the NAB decided to include a similar task (the Figure Drawing Test) within the Spatial Module of the NAB. However, only a copy and immediate recall condition was included in the published NAB, and therefore norms are available only for these two conditions. Had the authors also chosen to include a delayed recall condition for this measure during standardization and in the published NAB, this score could have potentially been used as an optional additional test to be transferred to the Memory Module in the event both Modules were given. It is believed that, had the authors chosen to do this, the overall sensitivity of NAB Memory Module to right temporal impairment would likely have increased.

The encouraging findings concerning the NAB's ability to predict localization of seizure focus in our study, however, should not be downplayed in light of its limitations in predicting laterality. The specific prediction of seizure localization is an important component of neuropsychological testing within epilepsy populations as localization of seizure focus more so than lateralization is more likely to be ambiguous from EEG data alone.

Future Directions for Research

While our findings provide some limited support for the clinical utility of the NAB within an epilepsy population, there is not enough information yet available to definitively determine its utility with this population. The current study evaluated concurrent validity using quantitative NAB indicators and did not involve a clinical judgment component (e.g., how NAB data would be used and interpreted within a multidisciplinary epilepsy management team). Future research

that would help to answer this question could focus on the NAB's ability to classify lateralization and localization of seizure focus when being clinically interpreted by a qualified neuropsychologist. In routine clinical practice, a neuropsychologist typically administers a battery of measures (such as the UF standard neuropsychological battery mentioned in Chapter One) and uses the scores from these measures to make predictions regarding lateralization and localization of seizure focus. Though the quantitative scores and subsequent derivations of such scores are heavily factored into these predictions, additional qualitative factors concerning patient performance (including observations regarding a patients' approach or process on particular measures) are also potentially contributory but were not included in the present study. Just as the NAB has focused on including ecologically valid Daily Living subtests within each Domain Module, it could be argued that the most ecologically valid method of determining the clinical utility of the NAB within an epilepsy population would involve providing a group of trained neuropsychologists with all available NAB data (including scores and raw data) from a sample of patients with known electrographic seizures of varying lateralizations (left vs. right vs. nonlateralizing) and localizations (temporal lobe vs. extratemporal) and assessing their rates of correct classification (and rates of interrater reliability) based on available EEG and magnetic resonance imaging (MRI) data. If these individuals demonstrated sufficient reliability and predictive ability to classify seizure lateralization and localization using NAB data, this would provide substantial support for the clinical utility of the NAB with this population. Additional studies could further compare the predictive ability of the NAB Screening Module alone compared with the five Core NAB Modules in a similar manner (using a trained neuropsychologists' clinical judgment) to further explore more time efficient and cost effective measures of neurocognitive assessment with this population.

Conclusion

In summary, our study provided some support for the clinical utility of the NAB within an epilepsy population. Specifically, our results suggested that certain combinations of NAB scores (as well as additional derived scores) were able to disseminate between individuals with temporal lobe epilepsy and individuals whose seizures originated outside the temporal lobe. Our results provided limited evidence, however, for the NAB's ability to successfully predict seizure laterality. Future research with the NAB (specifically, tests of the NAB's ability to predict lateralization and localization of seizure focus when the results are analyzed by one or more trained clinical neuropsychologists, similar to the techniques used in current practice with this population using other neuropsychological batteries) is warranted to more definitively determine its clinical utility within an epilepsy population.

LIST OF REFERENCES

- Abel, B. (2005). *Intractable epilepsy: When medication can't stop seizures*. Retrieved May 12, 2007, from <http://healthlink.mcw.edu/article/1031002476.html>
- Anastasi, A., & Urbina, S. (1997). *Psychological Testing (7th ed.)*. Newark, NJ: Prentice-Hall/Simon & Schuster.
- Beck, A.T., Steer, R.A., & Brown, G.K. (1996). *Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation.
- Benbadis, S.R. (2005). A spell in the epilepsy clinic and a history of “chronic pain” or “fibromyalgia” independently predict a diagnosis of psychogenic seizures. *Epilepsy Behavior*, 6, 264-265.
- Benbadis, S.R. (2010, September 21). *Psychogenic nonepileptic seizures*. Retrieved July 16, 2010, from <http://emedicine.medscape.com/article/1184694-overview>
- Brooks, B.L., Iverson, G.L., & White, T. (2007). Substantial risk of “Accidental MCI” in healthy older adults: Base rates of low memory scores in neuropsychological assessment. *Journal of the International Neuropsychological Society*, 13, 490-500.
- Brooks, B.L., Iverson, G.L., & White, T. (2009). Advanced interpretation of the Neuropsychological Assessment Battery with older adults: Base rate analyses, discrepancy scores, and interpreting change. *Journal of the International Neuropsychological Society*, 24, 647-657.
- Brown, L.B., Stern, R.A., Cahn-Wiener, D.A., Rogers, B., Messer, M.A., Lannon, M.C., Maxwell, C., Souza, T., White, T., & Ott, B.R. (2005). Driving scenes test of the Neuropsychological Assessment Battery (NAB) and on-road driving performance in aging and very mild dementia. *Archives of Clinical Neuropsychology*, 20, 209-215.
- Cahn-Weiner, D.A., Wittenberg, D., & McDonald, C. (2009). Everyday cognition in temporal lobe and frontal lobe epilepsy. *Epileptic Disorders*, 11, 222-227.
- Campbell, D.T., & Fiske, D. W. (1959). Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychological Bulletin*, 56, 81-105.
- Cicchetti, D.V., & Sparrow, S.S. (1981). Developing criteria for establishing interrater reliability of specific items: Applications to assessment of adaptive behavior. *American Journal of Mental Deficiency*, 86 (2), 127-137.
- Cleveland Clinic. (2007). *Adult epilepsy*. Retrieved May 12, 2007, from <http://cms.clevelandclinic.org/neuroscience/body.cfm?id=124>
- Corder, G.W., & Foreman, D.I. (2009). *Nonparametric Statistics for Non-Statisticians: A Step-by-Step Approach*. Hoboken, NJ: John Wiley & Sons.

- Delis, D.C., Kramer, J.H., Kaplan, E., & Ober, B.A. (2000). *California Verbal Learning Test-Second Edition (CVLT-II)*. San Antonio, TX: Psychological Corporation.
- Frings, L., Wagner, K., Unterrainer, J., Spreer, J., Halsband, U., & Schulze-Bonhage, A. (2006). Gender-related differences in lateralization of hippocampal activation and cognitive strategy. *Neuroreport*, *17* (4), 417-421.
- Gavett, B.E., Poon, S.J., Ozonoff, A., Jefferson, A.L., Nair, A.K., Green, R.C., & Stern, R.A. (2009). Diagnostic utility of the NAB List Learning test in Alzheimer's disease and amnesic mild cognitive impairment. *Journal of the International Neuropsychological Society*, *15*, 121-129.
- Golden, C.J., Purisch, A.D., & Hammeke, T.A. (1985). *Luria-Nebraska Neuropsychological Battery: Forms I and II*. Los Angeles, CA: Western Psychological Services.
- Goodglass, H. & Kaplan, E. (2000). *Boston Naming Test*. Philadelphia, PA: Lippincott, Williams & Wilkins.
- Grohman, K., & Fals-Stewart, W. (2004). The detection of cognitive impairment among substance-abusing patients: The accuracy of the Neuropsychological Assessment Battery-Screening Module. *Experimental Clinical Psychopharmacology*, *12* (3), 200-207.
- Halstead, W.C. (1947). *Brain and Intelligence*. Chicago, IL: University of Chicago Press.
- Heaton, R.K. (1981). *Wisconsin Card Sorting Test*. Odessa, FL: Psychological Assessment Resources, Inc.
- Iverson, G.L., Williamson, D.J., Ropacki, M., & Reilly, K.J. (2007). Frequency of abnormal scores on the Neuropsychological Assessment Battery Screening Module (S-NAB) in a mixed neurological sample. *Applied Neuropsychology*, *14*, 178-182.
- Janszky, J., Schulz, R., Janszky, I., & Ebner, A. (2004). Medial temporal lobe epilepsy: Gender differences. *Journal of Neurology, Neurosurgery, and Psychiatry*, *75* (5), 773-775.
- Klove, H. (1963). Clinical neuropsychology. In F.M. Forster (Ed.), *The medical clinics of North America*. New York, NY: Saunders.
- Lowe, N.K., & Ryan-Wenger, N.M. (1992). Beyond Campbell and Fiske: Assessment of convergent and discriminant validity. *Research in Nursing and Health*, *15*, 67-75.
- Martin, J. (2008, October 30). *The truth about psychogenic nonepileptic seizures*. Retrieved July 16, 2010, from http://www.epilepsy.com/articles/ar_1112967056
- Mayo Clinic. (2007). *Epilepsy treatment options*. Retrieved May 10, 2007, from <http://www.mayoclinic.org/epilepsy/treatment.html>

- McHugh, J.C., & Delanty, N. (2008). Epidemiology and classification of epilepsy: Gender comparisons. *International Review of Neurobiology*, 83, 11-26.
- Moser, D.J., Bauer, R.M., Gilmore, R.L., Dede, D.E., Fennell, E.B., Algina, J.J., Jakus, R., Roper, S.N., Zawacki, T.N., & Cohen, R.A. (2000). Electroencephalographic, volumetric, and neuropsychological indicators of seizure focus lateralization in temporal lobe epilepsy. *Archives of Neurology*, 57 (5), 707-712.
- Myers, J.E. & Myers, K.R. (2004). *Rey Complex Figure Test and Recognition Trial*. Odessa, FL: Psychological Assessment Resources, Inc.
- Owsley, C., Ball, K., Sloane, M. E., Roenker, D. L., & Bruni, J. R. (1991). Visual/cognitive correlates of vehicle accidents in older drivers. *Psychology and Aging*, 6, 403-415.
- Pilcher, W.H., Lochareernkul, C., Primrose, D., Ojemann, L.M., & Ojemann, G.A. (1992). Update in epilepsy III: Surgical therapy of intractable epilepsy. *New York State Journal of Medicine*, 92, 92-96.
- Reitan, R.M. (1958). Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and Motor Skills*, 8, 271-276.
- Reitan, R.M., & Wolfson, D. (1993). *The Halstead-Reitan Neuropsychological Test Battery*. Tucson, AZ: Neuropsychological Press.
- Schmitt, N., & Stults, D.M. (1986). Methodology reviews: Analysis of multitrait-multimethod matrices. *Applied Psychological Measurement*, 10, 1-22.
- Scoville, W.B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry*, 20, 11-21.
- Snyder, P.J. (1998). Epilepsy. In P.J. Snyder & P.D. Nussbaum (Eds.), *Clinical neuropsychology: A pocket handbook for assessment*. Washington, DC: American Psychological Association.
- Spielberger, C.D. (1968). *State-Trait Anxiety Inventory*. Odessa, FL: Psychological Assessment Resources, Inc.
- Spren, O. & Benton, A. (1977). *Neurosensory Center Comprehensive Examination for Aphasia*. Victoria, BC: University of Victoria Neuropsychology Laboratory.
- Stern, R.A., & White, T. (2003). *Neuropsychological Assessment Battery: Administration, Scoring, and Interpretation Manual*. Lutz, Fla: Psychological Assessment Resources, Inc.
- Temple, R.O., Zgaljardic, D.J., Abreu, B.C., Seale, G.S., Ostir, G.V., & Ottenbacher, K.J. (2009). Ecological validity of the Neuropsychological Assessment Battery Screening Module in post-acute brain injury rehabilitation. *Brain injury*, 23, 45-50.

- Tombaugh, T.N., Kozak, J., & Rees, L. (1999). Normative data stratified by age and education for two measures of verbal fluency: FAS and animal naming. *Archives of Clinical Neuropsychology, 14*, 167-177.
- Valton, L., & Mascott, C.R. (2004). What is the current role of a Wada test in the pre-surgical work-up of pharmacologically intractable epilepsy in adults? *Revue Neurologique, 160* (1), 164-169.
- Wechsler, D. (1997). *WAIS-III/WMS-III Technical Manual*. San Antonio, TX: The Psychological Corporation.
- Wechsler, D. (1987). *Wechsler Memory Scale-Revised Manual*. San Antonio, TX: The Psychological Corporation.
- White, T., & Stern, R.A. (2003). *Neuropsychological Assessment Battery: Demographically Corrected Norms Manual*. Lutz, FL: Psychological Assessment Resources, Inc.
- White, T., & Stern, R.A. (2003). *Neuropsychological Assessment Battery: Psychometric and Technical Manual*. Lutz, FL: Psychological Assessment Resources, Inc.
- White, T., & Stern, R.A. (2003). *Neuropsychological Assessment Battery: U.S. Census-Matched Norms Manual*. Lutz, FL: Psychological Assessment Resources, Inc.
- 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*, 575-583.
- Zgaljardic, D.J., & Temple, R.O. (2010). Reliability and validity of the Neuropsychological Assessment Battery-Screening Module (NAB-SM) in a sample of patients with moderate-to-severe acquired brain injury. *Applied Neuropsychology, 17*, 27-36.

BIOGRAPHICAL SKETCH

Bradley J. Daniels graduated *summa cum laude* with a Bachelor of Arts degree in psychology from the University of Central Florida in 2003. He soon relocated to Gainesville after being accepted into the clinical psychology doctoral program in the Department of Clinical and Health Psychology at the University of Florida. He received his Master of Science degree in 2005 and continued on with his doctoral pursuits. His graduate work focused primarily on clinical neuropsychology and his research focused primarily on the neuropsychology of epilepsy. His clinical interests include clinical neuropsychology, rehabilitation psychology, and forensic psychology. He recently completed an APA-approved neuropsychology internship offered through the University of Alabama Birmingham's Psychology Internship Training Consortium in Birmingham, Alabama, where he was awarded the C.J. Rosecrans psychology internship award, awarded annually to the intern who has demonstrated outstanding promise in the field of clinical psychology upon completion of the internship. He also greatly enjoys teaching and has taught psychology as an adjunct assistant professor in the Department of Social and Behavioral Sciences at Santa Fe College in Gainesville, Florida since 2006. He has published multiple anthology essays relating psychological principles to popular culture, a tool he regularly utilizes to enhance learning in the classroom. Currently, he is completing a 2-year postdoctoral fellowship in rehabilitation psychology at the James A. Haley Veterans' Hospital in Tampa, Florida.

In addition, Mr. Daniels has been happily married to his wife Tiffany since 2008. He resides in Lakewood Ranch, Florida with his wife and their rambunctious dog, Jack Daniels.