MEMORY DEFICITS IN PATIENTS WITH PSYCHOGENIC NON-EPILEPTIC SEIZURES WITH A HISTORY OF PSYCHOLOGICAL TRAUMA

by

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Abstract

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by

Nicole Thorn

Adviser: Humberto Lizardi, Ph.D.

Objective: Studies have shown that memory functioning in psychogenic non-epileptic seizure (PNES) patients is similar to epileptic seizure (ES) patients. However, the majority of studies have not controlled for mood and effort when assessing memory, and few studies have investigated the cause of the memory deficits in PNES patients. This study examined whether PNES and ES patients exhibited similar memory functioning after controlling for mood and effort. It also explored whether a history of psychological trauma correlated with the memory deficits PNES patients. **Method**: PNES patients (N = 54) were compared to age-, gender-, and education-matched temporal lobe epilepsy (TLE) control patients (N = 54) on measures of learning and memory. PNES patients with a history of psychological trauma (N = 27) were compared to PNES patients without a history of psychological trauma (N = 27) on measures of learning and memory. **Results**: PNES and TLE patients exhibited equivalent learning and memory

performance. There was no difference in memory functioning between PNES patients with and without a history of psychological trauma. Both groups demonstrated impairment as compared to published norms on learning and recall. **Conclusions**: PNES patients, similar to TLE patients, exhibit memory impairment as compared to norms. Psychological trauma does not appear to account for the memory impairment in PNES patients.

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INTRODUCTION

Overview of Psychogenic Non-epileptic Seizures

Psychogenic non-epileptic seizures affect a large percentage of patients referred for epilepsy video-EEG monitoring and can be a disabling condition. Non-epileptic seizures are episodes of altered movement, emotion, sensation, or experience that are similar to those episodes caused by epileptic seizures but are not accompanied by abnormal electrical discharges in the brain (Krumholz & Niedermeyer, 1983; Lesser, 1996). Non-epileptic seizures can result from physiological or psychological origins. Physiological non-epileptic seizures can have multiple causes such as autonomic dysfunction, cardiac arrhythmias, or hypoglycemia (Alsaadi & Marquez, 2005). Non-epileptic seizures of a psychological origin are generally termed psychogenic non-epileptic seizures (PNES), but historically have been called pseudoseizures, hysterical seizures, or psychogenic seizures (Francis & Baker, 1999). They are believed to represent a physical manifestation of psychological distress (Alsaadi & Marquez, 2005). PNES can result from a variety of psychological processes including: misinterpretation of physical symptoms, reinforced behavior patterns in cognitively impaired patients, response to acute stress without psychopathology, or psychopathologic processes such as anxiety disorders, posttraumatic stress disorder, dissociative disorders, conversion disorder, hypochondriasis, psychoses, or other somatization disorders. The most common psychiatric diagnoses to accompany PNES are somatoform disorders, particularly conversion disorder, in which symptoms originate from psychiatric origins but are expressed through neurological symptoms (Alsaadi & Marquez, 2005; Bourgeois, Chang, Hilty, & Servis, 2002; Chabolla, Krahn, So, & Rummans, 1996; Riggio, 1994).

Patients with conversion symptoms are not consciously aware of their symptoms and are not intentionally producing them, such as in malingering or factitious disorders (Chabolla et al., 1996; Folks, Ford, & Regan, 1984). Despite the lack of abnormal brain electrical activity, patients with PNES often have more frequent, disabling seizures than patients with epileptic seizures (ES; E. Barry et al., 1998; Francis & Baker, 1999). PNES are difficult to distinguish from ES and errors in diagnosis are common (Francis & Baker, 1999; Kuyk, Leijten, Meinardi, Spinhoven, & Van Dyck, 1997).

Epidemiology

It is estimated that 5-33% of outpatients with intractable epilepsy and 10-50% of patients admitted for monitoring to specialty epilepsy centers suffer from PNES (Arnold & Privitera, 1996; Benbadis, Lancman, King, & Swanson, 1996; Bowman, 1998; R. J. Brown & Trimble, 2000; Chabolla et al., 1996; L. M. Cohen, Howard, & Bongar, 1992; Cragar, Berry, Fakhoury, Cibula, & Schmitt, 2002; Fakhoury, Abou-Khalil, & Newman, 1993; Francis & Baker, 1999; Gates, Ramani, Whalen, & Loewenson, 1985; Krumholz & Niedermeyer, 1983; Kuyk et al., 1997; Leis, Ross, & Summers, 1992b; Lesser, Lueders, & Dinner, 1983; Meierkord, Will, Fish, & Shorvon, 1991; Walczak et al., 1995). In the general population, it is estimated that 1.4-33 out of every 100,000 people suffers from PNES (Benbadis, Agrawal, & Tatum, 2001; Francis & Baker, 1999; Sigurdardottir & Olafsson, 1998). Of these patients, 70-85% are female; however studies indicate that few socio-demographic differences exist between male and female PNES patients with the exception of an increased history of sexual abuse in women (Francis & Baker, 1999; Krumholz & Niedermeyer, 1983; Kuyk et al., 1997; Lesser, 1996; Meierkord et al., 1991; Oto, Conway, McGonigal, Russell, & Duncan, 2005; Rechlin, Loew, & Joraschky, 1997;

Walczak et al., 1995). It is hypothesized that the increased incidence of PNES in women is accounted for by a variety of sociologic and cultural factors including economic and social restraints for women in society. Women generally experience socialization that discourages the expression of anger, violence, competitiveness, and sexuality and, subsequently, may convert these repressed energies into physical symptoms, conversion reactions, or dissociative reactions (Bowman, 1993; Bowman & Markand, 1996; Francis & Baker, 1999; Lazare, 1981; Stefanis, Markidis, & Christodoulou, 1976; Ziegler, Imboden, & Meyer, 1960). While PNES are rare in the general population, they are quite frequent in epilepsy center populations and pose a major challenge for health care providers in their attempts to provide appropriate treatment.

Risk Factors

Psychological Trauma

The most common risk factor for PNES patients is a history of psychological trauma. Eighty six to eighty eight percent of patients with PNES reported a history of trauma as compared to 36% of epilepsy patients (Arnold & Privitera, 1996; Bowman, 1993). Patients with PNES have reported a variety of trauma types that occur in both childhood and adulthood. Physical and sexual abuse are particularly common, with estimates of childhood sexual abuse in PNES patients ranging from 24-67% as compared with 6-38% in the general population. It is estimated that 29% of PNES patients reported being raped during adulthood and 22% reported having a sexually abusive spouse (marital rape). Estimates of childhood physical abuse in PNES patients range from 15-71% compared to 5-13% in the general population, and 40% of patients reported having a

physically abusive spouse (resulting in injury; Alper, Devinsky, Perrine, Vazquez, & Luciano, 1993; Bowman, 1993, 2000; Bowman & Markand, 1996; Francis & Baker, 1999; Rosenberg, Rosenberg, Williamson, & Wolford, 2000; Sirven & Glosser, 1998; Tojek, Lumley, Barkley, Mahr, & Thomas, 2000; Wood, Haque, Weinstock, & Miller, 2004). Psychological abuse and stressful environments and/or inadequate family settings that affect a patient's subjective perception of well-being are also common in PNES patients (Wood et al., 2004). In addition to abuse, other types of trauma are reported by 28-60% of PNES patients with examples including serious falls, car accidents, witnessing murder or traumatic death of loved ones, cancer, adulthood torture, and abduction. Patients with PNES have higher rates of PTSD as compared with epilepsy patients (Rosenberg et al., 2000). It has been postulated that abuse may lead to dissociative reactions that mimic seizures (Bowman, 1993; Bowman & Markand, 1996; Francis & Baker, 1999). These data reinforce the notion that psychological trauma, or experiencing an extremely stressful life event, can precipitate the development of PNES.

Stress

Based on these and other findings, stress is likely an etiological factor in the development of PNES, and Wood et al. (2004) argue that PNES are more accurately conceptualized as "stress-related seizures," citing McEwen's model of allostasis and allostatic load as an explanation (McEwen, 1998). This model postulates that the autonomic nervous system (ANS), hypothalamic-pituitary-adrenal (HPA) axis, and immune systems are activated simultaneously to ready an organism for an adaptive response in the face of an internal or external, physical, psychological, or emotional

challenge. During this process, the bodily requirements needed for a response bring forth psychobiologic changes that place a "load" on various physiological systems within the organism (allostatic load), such as prolonged increases in blood pressure, excessive release of stress hormones (catecholamines and glucocorticoids), and prolonged decreases in insulin. During periods of repeated or chronic stress, the organism experiences physiological and emotional dysregulation, increasing susceptibility to illnesses such as hypertension, diabetes, and vascular disease. Additionally, repeated and prolonged stress can have negative effects on the brain, especially the hippocampus, due to the high concentration of glucocorticoid receptors in the hippocampus. Wood et al. (2004) argue that PNES may result as a product of this process.

Other Risk Factors and Comorbidity

In addition to stress and psychological trauma, other risk factors may predispose people to developing PNES. For example, 20-30% of PNES patients report previous mild head trauma (E. Barry et al., 1998; Devinsky et al., 1996; Francis & Baker, 1999). While there is some inconsistency, a family history of epilepsy may also be a risk factor for developing PNES (R. J. Brown & Trimble, 2000; Cragar et al., 2003; Stewart, Lovitt, & Stewart, 1982). Furthermore, the psychosocial precipitants seen in conversion disorder are common risk factors for PNES including: living in rural settings, having lower socioeconomic status, and having less knowledge regarding medical and psychological concepts (*Diagnostic and Statistical Manual of Mental Disorders*, 2000). Additionally, a personal and family history of psychiatric illness and the presence of comorbid psychopathology are more common in patients with PNES as compared to patients with

epilepsy (Bowman & Markand, 1996; R. J. Brown & Trimble, 2000; Kanner et al., 1999; Krishnamoorthy, Brown, & Trimble, 2001; Ozkara & Dreifuss, 1993; Stewart et al., 1982; Wyllie, Glazer, Benbadis, Kotagal, & Wolgamuth, 1999). Rechlin et al. (1997) reported that in an analysis of 18 PNES patients, 28% suffered from major depression, 39% from eating disorders, 39% from substance abuse, and 67% had made suicide attempts. Additionally, reports have indicated a high comorbidity between PNES and anxiety; panic attacks; somatoform disorders (mainly conversion disorder); PTSD; dysthymia, chronic pain; borderline, antisocial, and histrionic personality disorders; and mild mental retardation (Alper, Devinsky, Perrine, Vazquez, & Luciano, 1995; Bowman, 1999; Dworetzky et al., 2005; Galimberti et al., 2003; Krishnamoorthy et al., 2001; Rechlin et al., 1997; Szaflarski, Ficker, Cahill, & Privitera, 2000; Thompson, 1992; Wood et al., 2004). Finally, patients with PNES also demonstrate elevations on the Minnesota Multiphasic Personality Inventory-2 (MMPI-2; Butcher, Dahlstrom, Graham, Tellegren, & Kraemmer, 1989) that follow a 3-1-2 pattern (Hypochondriasis, Depression, and Hysteria respectively; M. C. Brown, Levin, Ramsay, Katz, & Duchowny, 1991; Derry & McLachlan, 1996; Wilkus, Dodrill, & Thompson, 1984). While there may be physiological precipitants, many of the comorbidity findings provide further support that patients with PNES suffer from psychological stress.

Diagnosis of PNES

Diagnosis of PNES can be challenging and is usually made through a combination of clinical observation, video-electroencephalogram (V/EEG) monitoring, measurement

of serum prolactin levels, and/or neuropsychological assessment (Francis & Baker, 1999).

EEG and Seizure Induction

Routine EEG done as an outpatient is generally inadequate for distinguishing epilepsy from PNES for several reasons: seizures rarely occur during the test, there is a limited sample of recorded activity, high false negative rates are common, and seizure activity can be difficult to differentiate from movement artifact (Boon & Williamson, 1993; Cragar et al., 2002; Devinsky et al., 1996). Video-EEG monitoring (24-hour V/EEG monitoring with simultaneous video recording) is currently considered the "gold standard" for distinguishing PNES from ES (Krumholz, 1999). PNES is generally diagnosed when a patient demonstrates what is reported to be a "typical seizure," but no ictal EEG discharges are observable on the EEG recording at the time of the patient's seizure and other physiological causes have been ruled-out (Bare, Burnstine, Fisher, & Lesser, 1994; R. J. Brown & Trimble, 2000; Kuyk et al., 1997; Lesser, 1996). One of the difficulties with V/EEG is that patients may not experience normal events while being monitored, especially when intervals between seizures are long (R. J. Brown & Trimble, 2000; Kuyk et al., 1997). In addition, it may be difficult to detect EEG discharges from some partial seizures, especially those originating from the frontal lobes, and as a result, ES could be mistaken for PNES (Bare et al., 1994). Finally, epileptic-like interictal EEG patterns can occur in up to 3% of healthy people (R. J. Brown & Trimble, 2000; Fenton, 1986), which can be misleading.

In the event that patients do not experience a spontaneous seizure during 24-hour V/EEG monitoring, there are several other methods to aid in distinguishing ES from PNES. In patients with epilepsy, sleep deprivation or photic stimulation may provoke an ES (R. J. Brown & Trimble, 2000). In patients suspected of having PNES, the physician can also attempt to suggest or induce a seizure as PNES are more likely to be provoked by emotional stimuli and suggestion (R. J. Cohen & Suter, 1982). Induction techniques can include strong suggestion by the physician along with one or more of the following: injection of saline solution, placing a tuning fork on the body or head, or placing a pad soaked with alcohol on the neck. If the patient has a typical event during V/EEG monitoring as a result of these tests, then the diagnosis of PNES is given (Bazil et al., 1994; L. M. Cohen et al., 1992; R. J. Cohen & Suter, 1982; Francis & Baker, 1999; Krumholz & Niedermeyer, 1983; Kuyk et al., 1997; Lancman, Asconape, Craven, Howard, & Penry, 1994a; Slater, Brown, Jacobs, & Ramsay, 1995; Walczak, Williams, & Berten, 1994). However, it is sometimes possible to suggest an ES in epilepsy patients, which can lead to misdiagnosis (R. J. Brown & Trimble, 2000).

Evaluating Seizure Characteristics

Evaluation of seizure characteristics can also contribute to the differentiation of PNES from ES. For example, ES typically last between one to two minutes, whereas PNES often last longer than two minutes (M. C. Brown et al., 1991; Devinsky et al., 1996; Guberman, 1982; Meierkord et al., 1991; Slater et al., 1995). The nature of the convulsive activity sometimes differs between patients. PNES patients often display more purposeful, semipurposful, asymmetric, or asynchronous (thrashing or writhing

motion, not tonic-clonic) movements (Francis & Baker, 1999; Gates et al., 1985; Gulick, Spinks, & King, 1982; Leis et al., 1992b). The onset of PNES may be more gradual, they may display a waxing and waning course, and they may have excessive movements of the limbs, trunk, and head (J. J. Barry & Sanborn, 2001; Gates et al., 1985; Groppel, Kapitany, & Baumgartner, 2000; Gulick et al., 1982; Lancman, Brotherton, Asconape, & Penry, 1993; Meierkord et al., 1991; Reuber et al., 2003a). While PNES patients can have alterations in consciousness, they are often more conscious and responsive than ES patients during a seizure (R. J. Brown & Trimble, 2000; Francis & Baker, 1999; Gates et al., 1985; Gulick et al., 1982; Meierkord et al., 1991; Peguero, Abou-Khalil, Fakhoury, & Mathews, 1995; Reuber et al., 2003a; Wilkus et al., 1984). Additionally, crying and weeping are more common during PNES, as well as carpet burns and eye closure. While PNES patients frequently report self-injury and incontinence during seizures, they are rarely witnessed (Bergen & Ristanovic, 1993; R. J. Brown & Trimble, 2000; Chung, Gerber, & Kirlin, 2006; Francis & Baker, 1999; Peguero et al., 1995; Walczak & Bogolioubov, 1996). Finally, PNES patients often report that the onset of their seizures was later in life than that of epilepsy patients, and antiepileptic drug (AED) treatments are less effective in reducing their seizure frequency (Breier et al., 1998; M. C. Brown et al., 1991; R. J. Brown & Trimble, 2000; Derry & McLachlan, 1996; Frances, Baker, & Appleton, 1999; Gatzonis, Siafakas, Chioni, Zournas, & Mantouvalos, 1999; Howell, Owen, & Chadwick, 1989; Krumholz & Niedermeyer, 1983; Kuyk et al., 1997; Lesser, 1996; Meierkord et al., 1991; Ramchandani & Schindler, 1992; Saygi, Katz, Marks, & Spencer, 1992; Storzbach, Binder, Salinsky, Campbell, & Mueller, 2000; Walczak et al., 1995; Wilkus et al., 1984). In summation, while ES and PNES can have very similar

characteristics, because PNES are not caused by abnormal electrical discharges in the brain, their physical characteristics may be slightly to dramatically different.

Measuring Prolactin Levels

Measuring serum prolactin immediately following a seizure can be an additional diagnostic indicator when attempting to distinguish ES from PNES; however, it is limited to certain seizure types. Prolactin levels rise 5-10 fold following tonic-clonic seizures, and they rise slightly less following complex-partial seizures (R. J. Brown & Trimble, 2000; Francis & Baker, 1999; Meierkord, Shorvon, Lightman, & Trimble, 1992; Pritchard, Wannamaker, Sagel, Nair, & DeVillier, 1983; Trimble, 1986).

Summary

Overall, distinguishing ES from PNES can be very difficult. Because of this, it is important to understand the characteristics, epidemiology, and risk factors associated with PNES. Familiarity with various diagnostic tools in combination with having a thorough understanding of PNES will ultimately result in a greater probability of accurate diagnosis and effective treatment.

Treatment of PNES

It is generally recommended that patients diagnosed with PNES participate in psychotherapy to address the psychological issues underlying their disorder. Patients will typically receive psychoeducation, psychotherapeutic intervention, and possibly medication. Family and/or couples therapy is often helpful in addressing stressors in the patient's environment. Studies generally have not investigated the effectiveness of specific interventions, but psychotherapy in general appears to be effective in reducing or

eliminating PNES (J. J. Barry & Sanborn, 2001; Lesser, 1996). Additionally, counseling conducted by physicians associated with a comprehensive epilepsy center appears to be more effective then counseling conducted by an outside physician (Aboukasm, Mahr, Gahry, Thomas, & Barkley, 1998).

Neuropsychological Performance in PNES Patients

In addition to the procedures mentioned above, neuropsychological testing is often used to aid in the differential diagnosis between epileptic and non-epileptic seizures. However, patients with PNES often have deficits similar in nature to ES patients, indicating the need for further understanding of this diagnostic tool. Neuropsychological testing generally examines intellectual ability and performance in various areas of cognitive functioning, such as, language, attention and concentration, executive functioning, visual-spatial functioning, and memory. Understanding memory functioning in PNES patients is particularly critical as this is the most commonly reported deficit in this population.

General Intelligence

With regard to discrimination between ES and PNES groups based on intellectual performance, some inconsistency exists in the literature. In early studies (i.e. prior to ~1990), PNES patients performed better on performance, verbal, and full scale IQ (PIQ, VIQ, and FSIQ) measures (Matthews, Shaw, & Klove, 1966; Sackellares et al., 1985; Stewart et al., 1982). However, it is important to note that the study by Matthews, Shaw, and Klove (1966) examined intellectual performance in a group that was not a pure PNES group, but contained patients with a variety of pseudo-neurologic symptoms. Only one

contemporary study by Dodrill and Holmes (2000) supported earlier findings of lower VIQ and FSIQ in ES patients as compared to PNES patients. However, both groups scored in the low end of the average range and there was only a 4-point difference in both VIQ and FSIQ means between the two groups. Additionally, the authors did not control for comorbid neurologic diagnoses which may have confounded the findings. Instead, they proposed that the findings seen in both groups may have been due to unknown positive neurologic histories (Dodrill & Holmes, 2000). All other recent studies using the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981) indicated no differences on VIQ, PIQ, FSIQ, or selected subtests between ES and PNES patients. In general, scores on the WAIS-R ranged from the low 80's to low 90's for both ES and PNES groups (Derry & McLachlan, 1996; Drake, Huber, Pakalnis, & Phillips, 1993; Kalogjera-Sackellares & Sackellares, 1999). Binder, Kindermann, Heaton, & Salinsky (1998) also reported that both the ES and the PNES groups scored significantly lower on IQ measures as compared with normal controls though neither group mean fell below the average range. Further strengthening the validity of the more recent findings, the majority of these contemporary studies controlled for comorbid neurologic diagnoses such as stroke, lesions, tumors, birth trauma, infections, brain surgery and degenerative brain disorders (Binder et al., 1998; Bortz, Prigatano, Blum, & Fisher, 1995; Breier et al., 1998; M. C. Brown et al., 1991; Drake et al., 1993; Kalogjera-Sackellares & Sackellares, 1999; Swanson, Springer, Benbadis, & Morris, 2000). Finally, one report of patients with both ES and comorbid PNES indicated lower overall IQ's in the comorbid group than patients with ES alone, but they did not report controlling for comorbid neurologic diagnoses (Reuber et al., 2003b).

Halstead-Reitan Battery

Studies of neuropsychological performance, using a variety of measures, have indicated that PNES patients have a range of neuropsychological deficits, and that many of their impairments are similar to those seen in epilepsy patients. To examine cognitive performance in PNES patients, many studies have used the Halstead-Reitan Neuropsychological Test Battery (HRB; Reitan & Wolfson, 1993) or selected subtests from this battery. While several studies have indicated that PNES patients perform better than ES patients on multiple measures within the battery, PNES patient's performance was still suggestive of cognitive impairment. For example, Sackellares et al. (1985) compared a PNES group to a group with both PNES and comorbid ES and found that while the PNES group performed better than the ES plus PNES group on all IQ and cognitive measures, the PNES patients performed more poorly on neuropsychological measures than would be expected for people with equivalent intelligence levels. The mean Halstead Impairment (HI) index (which reflects overall level of neuropsychological performance) for the PNES group was also in the borderline range between normal and impaired brain function. Another study by this group (Kalogjera-Sackellares & Sackellares, 1999), also comparing PNES patients to patients with PNES plus ES, found that while a significantly higher percentage of PNES plus ES patients (75%) scored in the impaired range on the HI index, more than half (61%) of the PNES patients also scored in the impaired range. This suggests that many PNES patients demonstrate impairment in neuropsychological performance. However, it is important to note that because the control groups in both of these studies consisted of patients with ES and comorbid PNES, conclusions from this literature are difficult to draw.

Wilkus & Dodrill (1989) used select subtests from the HRB to compare 25 PNES patients to three different ES groups. The first two ES groups were a partial epilepsy group and a generalized epilepsy group (A and B), matched on several demographic variables including age, gender, and education. The third ES group, a generalized epilepsy group (C), was matched to the PNES group on age and gender, but had an average of 2.4 fewer years of education. Results indicated that the generalized epilepsy group (C), which had less education, performed more poorly than the PNES group on several measures from the battery, including the HI index. However, there were no differences in neuropsychological performance between the PNES group and the partial epilepsy group or the generalized epilepsy group (A and B). PNES patients demonstrated significant neuropsychological impairment (defined as more than half of the test scores outside the normal limits) as often as the ES patients, but the authors do not report the percentage of patients who scored in the impaired range in each group (Wilkus & Dodrill, 1989). Finally, Dodrill & Holmes (2000) compared 100 PNES and 100 ES patients, matched on all demographic variables, and found that while there were some differences in neuropsychological performance, these differences were very slight and of no practical use for distinguishing the two groups. Both groups performed at the low end of average on intelligence testing and both showed mild, but definite neuropsychological impairment. This was especially true for memory performance in which they found no differences between groups. Both groups were below average and outside the normal limits in comparison to test norms.

Verbal and Nonverbal Memory Functioning

As indicated above, studies using the HRB imply that many patients with PNES demonstrate impairment in neuropsychological performance because they are equivalent to ES patients, and ES patients, particularly those with temporal lobe epilepsy (TLE), exhibit hippocampal degeneration and learning and memory impairments (Hattiangady & Shetty, 2008). Memory, in particular, appears to be impaired since results indicated no global differences between PNES and ES patients on measures assessing memory. While there is some variability, studies utilizing tests of memory functioning (other than those used in the HRB) have generally indicated no differences in either verbal or nonverbal memory between PNES and ES patients. For example, studies using the Wechsler Memory Scale (WMS; Wechsler, 1945) and the Wechsler Memory Scale – Revised (WMS-R; Wechsler, 1987) have reported no differences between ES and PNES patients in either verbal memory, as measured by the Logical Memory and Paired Associations subtests, or in nonverbal memory, as measure by the Visual Reproduction subtest (Binder et al., 1998; M. C. Brown et al., 1991; Slater et al., 1995; Swanson et al., 2000). Most of these studies reported mean raw scores and suggested that PNES patients were impaired in memory functioning because their scores were similar to ES patients, a group with known memory deficits. However, they generally did not compare subject's scores to population norms, so their degree of impairment is unclear. Similar results were also found utilizing other measures of verbal memory including the Rey Auditory Verbal Learning Test (Rey AVLT; Rey, 1964) and the Selective Reminding Test (Buschke, 1973). Studies using the Benton Visual Retention Test (BVRT; A. Benton, 1965) and the 7/24 Spatial Recall Test (Rao, Hammeke, McQuillen, Khatri, & Lloyd, 1984), both

measures of nonverbal memory, reported no differences between ES and PNES patient groups (Binder et al., 1998; M. C. Brown et al., 1991; Slater et al., 1995; Swanson et al., 2000). While several studies reported the percentage of patients who scored in the impaired range, they did not distinguish which test scores from the battery were actually impaired; so it is difficult to know if memory performance in particular is impaired as compared to published norms. Finally, Reuber et al. (2003b) compared patients with PNES plus comorbid ES to patients with ES only and reported no differences on verbal memory, as measured by the VLMT (Verbaler Lern- und Merkfähigkeitstest; Verbal Learning and Memory Test; Helmsteadter, Lendt, & Lux, 2001), as well as no differences on nonverbal memory, as measured by the DCS (Diagnostikum für Cerbralschädigung; Diagnosis of Cerebral Damage; Lamberti, 1999). Again, the use of a control group with ES and comorbid PNES confounds the study because it is difficult to make comparisons between ES and PNES. It is important to note that the studies reviewed above used epilepsy control groups that consisted of either generalized epilepsy or a combination of partial and generalized epilepsy. When investigating memory deficits, a temporal lobe epilepsy (TLE) control group is preferable because seizures (and associated neuronal damage) are more specific to the temporal lobe, which houses the hippocampus, and hippocampal damage and memory deficits are common in TLE (Devinsky, 2004). This contrasts to other types of partial (e.g., multifocal epilepsy in which abnormal electrical activity can arise from both hemispheres and/or many different parts of the brain) and/or generalized (where epileptic activity arises throughout the brain simultaneously) seizures. Because the abnormal activity may stem from or travel to many different brain regions,

these patients may have more global and variable cognitive and neuropsychological deficits, skewing the memory findings in this type of patient control group.

Despite these reports that there are no significant differences between PNES and ES patients on memory functioning, three studies reported contradictory findings. Breier et al. (1998) found that PNES patients scored significantly higher on the Verbal (Buschke & Fuld, 1974) and Non-Verbal (Fletcher, 1985) Selective Reminding Tests than patients with right TLE (RTLE) and left TLE (LTLE). This is one of the few studies to compare scores to population norms. It is important to note that LTLE patients were in the impaired range ($z = -2.3$) and RTLE patients were in the low average range ($z = -1.0$) as compared to PNES patients who were in the average range ($z = -0.6$) on the Verbal Selective Reminding Test. On the Non-Verbal Selective Reminding Test, all groups scored within the average range despite significant differences between the RTLE and PNES groups. Another study reported that PNES patients performed significantly better than ES patients who were candidates for epilepsy surgery on the Verbal and Design Recall subtests of the WMS (Novelly, 1993). Finally, Locke, Berry, Fakhoury, & Schmitt (2006) reported what they described as an unexpected finding in which the memory composite score was significantly more impaired in ES patients, than PNES patients. However, the composite score was created from the Wechsler Memory Scale-III (WMS-III; Wechsler, 1997b) immediate and general memory scores and is not ideal because the immediate memory score on the WMS-III is part of the general memory score; so combining those two scores essentially incorporates the immediate memory score into the composite twice. It is also difficult to interpret this finding; while they

reported that the PNES patient's composite memory score was 6 points lower than the ES patients, they did not report the differences between scores on individual tests or compare the scores to normative means. In summary, despite some inconsistency in performance, both the HRB and various other measures specifically designed to assess memory functioning suggest the presence of verbal and nonverbal memory deficits in PNES patients.

Due to similar performance between ES and PNES groups on measures assessing verbal memory, Bortz et al. (1995) investigated differences between the two groups in response characteristics on the California Verbal Learning Test (CVLT; Dellis, Kramer, Kaplan, & Ober, 1987). Results indicated that PNES patients showed a negative response bias (failure to recognize originally presented material) as compared with LTLE patients who showed a positive response bias (recognition of material not in the original presentation). A negative response bias is generally less common in patients with mild to moderate memory impairment secondary to neurologic disease. Because of this, the authors suggested that the patient's reduced scores on the CVLT might have been due to something other than memory impairment. They speculated that the negative response bias might have reflected the psychological defense mechanism of denial rather than organic brain dysfunction because patients did not verbally report or explicitly recognize information repeatedly presented to them. However, the authors provide no support for this hypothesis. They also argue that depression in the PNES group most likely does not account for the negative response bias seen in this group. They state that although memory complaints are common in people with depression, and comorbidity between

depression and PNES is high, comorbidity between depression and epilepsy is also high and their TLE control group did not demonstrate a negative response bias (Bortz et al., 1995). Despite this argument, due to the comorbidity between PNES and depression, it is important to control for depression when investigating memory deficits in PNES patients.

Additional Neuropsychological Functioning

Studies examining other domains of neuropsychological performance, using a variety of different tests, have generally concluded that there are no differences in test performance between patients with PNES and those with ES. In fact, one study by Reuber et al. (2003b) even found that PNES patients performed more poorly on neuropsychological measures than ES patients. They reported that patients with ES plus comorbid PNES had significantly more global neuropsychological impairment than the patients with ES alone. Global neuropsychological impairment was defined as abnormal or highly abnormal performance on all parts of the testing procedure. They hypothesized that impairments might have been related to the high risk of sexual and physical abuse (also a risk factor for patients with PNES) in people with learning disabilities. This is notable because people with learning disabilities also have impairments in neuropsychological functioning (Elvik, Berkowitz, Nicholas, Lipman, & Inkelis, 1990; Furey, 1994). It may be that the impaired neuropsychological performance seen in patients with PNES is the result of a comorbid learning disability.

Similarly, studies using the Neuropsychological Battery for Epilepsy (Dodrill, 1978) found no differences between PNES and ES patients on any measure of cognitive or neuropsychological functioning. Furthermore, both PNES and ES patients scored

outside the normal limits on approximately 50% of tests from the battery (Dodrill, Wilkus, & Batzel, 1993; Wilkus et al., 1984). Several additional studies showed no differences between PNES and ES groups in language, attention and concentration, executive functioning, visual-perception abilities, or motor functioning (Binder et al., 1998; Breier et al., 1998; M. C. Brown et al., 1991; Locke, Berry, Fakhoury, & Schmitt, 2006; Slater et al., 1995; Swanson et al., 2000). Of these studies, only one utilized a normal control group in addition to an ES group, and the normal control group was only administered a portion of the battery. However, the available results indicated that the normal controls performed significantly better than the ES and PNES groups on all measures administered. Additionally, while M. C. Brown et al. (1991) reported that 60% of PNES patients scored within the mildly to severely impaired range, none of the studies reported above compared the patient's test scores to the normative population means, so it is difficult to interpret which test scores were impaired in PNES and ES patients.

Despite prevalent findings that impairment in PNES patients on neuropsychological measures is similar to impairment seen in ES patients, the results of a few studies report differences between the two patient groups on some select measures. Binder, Salinsky, & Smith (1994), Reuber et al. (2003b), and Risse, Mason, & Mercer (2000) reported differences between PNES groups and ES groups on the Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983), Finger Agnosia (Reitan & Wolfson, 1985), Controlled Oral Word Association Test (A. L. Benton & Hamsher, 1989), and Design Fluency (Regard, Strauss, & Knapp, 1982), with ES patients demonstrating more impairment than PNES patients (Binder et al., 1994; Reuber et al., 2003b; Risse et al.,

2000). Despite these select findings, results generally indicated significant impairment in all areas of neuropsychological functioning in the PNES group. However, it is still unclear as to the cause of these impairments since patients with PNES do not exhibit the specific neurological damage secondary to seizure activity seen in ES patients.

Contribution of Effort, Psychopathology, and Neuropathology to Functioning

What accounts for the neuropsychological deficits seen in PNES patients? Swanson et al. (2000) suggested that psychiatric disturbances along with variable effort and attentional deficits in PNES patients may account for their poor test performance. Reuber et al. (2003b) speculated that low IQ or global neuropsychological deficits lead to an increased risk for developing PNES because they may have limitations in their problem-solving and communication skills or limitations in their ability to communicate distress. However, it is difficult to know if neuropsychological deficits lead to the development of PNES or if developing PNES results in the development of neuropsychological deficits. M. C. Brown et al. (1991) and Slater et al. (1995) reported that performance on neuropsychological measures was inconsistent, with PNES patients failing easy items and completing more difficult items, or recalling more information on delayed recall conditions than they recalled immediately following a presentation. The authors hypothesized that the inconsistent performance on tests may indicate psychological rather than organic factors as the cause for impairments. In addition, they raised the possibility that inconsistent effort may account for these patterns in test performance (M. C. Brown et al., 1991; Slater et al., 1995).

Few studies examining neuropsychological performance in patients with PNES have included measures of effort as part of their test battery or examined correlations between effort and neuropsychological functioning. In addition, while many studies have included tests assessing psychological functioning (e.g. MMPI), few have examined correlations between psychological functioning and performance on neuropsychological measures. Finally, few studies have controlled for the possibility that neurological history may contribute to the neuropsychological deficits seen in PNES patients. Binder et al. (1994) reported PNES patients scored significantly lower on the Portland Digit Recognition Test (PDRT; Binder, 1993), a measure of effort, than the ES patients. In a separate study, neuropsychological functioning was more strongly correlated with the PDRT in PNES patients than in ES patients. Additionally, while MMPI-2 scales explained little variance in neuropsychological performance in either ES or PNES patients, there were group differences on scales 1 and 3 (Depression and Hypochondriasis), but the direction of the relationship was not reported (Binder et al., 1998). Based on these results, Binder et al. (1998) concluded that impairment was more strongly associated with emotional and psychosocial factors in the PNES group than in the ES group. Locke, Berry, Fakhoury, & Schmitt (2006) reported that poor effort on the Test of Memory Malingering (TOMM; Tombaugh, 1996) was predictive of poorer memory functioning in both ES and PNES groups and that "effort" did not distinguish groups. They also reported that psychopathology was correlated with poorer neuropsychological functioning in both PNES and ES patients. In addition, neuropathology, as measured by neurological exam, MRI, and a history of neurological insults, was correlated with poorer memory functioning in both groups. This combined

pattern suggests that psychopathology and neuropathology are not distinguishing factors for neuropsychological impairment between the two groups. Finally, using four measures of effort, the TOMM, the Digit Memory Test (Hiscock & Hiscock, 1989), the Letter Memory Test (Inman & Berry, 2002), and the PDRT, researchers found that 22% of ES patients and 24% of PNES patients scored below the criteria for poor effort on one or more measures (Cragar, Berry, Fakhoury, Cibula, & Schmitt, 2006). Taken together, these findings indicate that poor effort, psychopathology, and neuropathology may all be contributing factors in the reduced neuropsychological performance seen in PNES patients. However, these three factors may also contribute to impaired performance in ES patients. The results highlight the need for measures of effort in both studies and clinical settings that involve ES and PNES patients. In addition, it highlights the need for further exploration of additional factors that are predictive of neuropsychological functioning in patients with PNES.

Summary

Reviewing the findings collectively, it seems that despite some inconsistent results, patients with PNES may suffer from impairments in neuropsychological functioning, and in particular, they tend to demonstrate significant memory impairments. It should be noted that studies investigating memory functioning in PNES patients have various limitations. For example, many studies do not compare their results to population norms and many studies utilize control groups composed of patients with mixed seizure types; however, no particular limitation or pattern of limitations seems to explain the inconsistent findings. Additionally, while psychopathology, neuropathology, and effort

help explain some of the variance in cognitive functioning, a large portion of the variance is still unaccounted for. For example, studies of neuropsychological functioning have yet to explore one of the major risk factors for developing PNES: a history of psychological trauma and its impact on cognitive functioning. In order to understand the effect of psychological trauma on cognitive functioning it is important to examine the effect of stress on the brain as it relates to memory.

Memory: Neuroanatomy, Psychobiology, and Stress

Neuroanatomy of Memory

Many of the brain regions involved in memory are also involved in the stress response. Sensory information from the primary sensory cortices enters through the thalamus and travels to the hippocampus, amygdala, neocortex, and other areas of the brain. Long-term storage occurs mainly in the primary sensory cortical areas (Bremner, Krystal, Southwick, & Charney, 1995c). Implicit memory functions are mediated by the neocortex, and emotional memories are mediated by the amygdala and prefrontal cortex. The hippocampus along with adjacent cortical areas, the thalamus, and the prefrontal cortex are responsible for explicit memory encoding and consolidation (Bremner et al., 1995c). The hippocampus is a bilateral subcortical structure, with laminar organization, located in the temporal lobe. It receives inputs from the entorhinal cortex that form synapses on granule neurons in the dentate gyrus. These neurons then send projections to the CA3 pyramidal neurons that in turn project onto CA2 and CA1 neurons. Projections then go outside the hippocampus. The hippocampus is involved in the consolidation of short-term memory into long-term explicit memory, as well as, spatial learning and

behavior inhibition (Sapolsky, 2000; Weber & Reynolds, 2004). Stress affects the hippocampus by changing its cytoarchitecture, which may result in deficits in explicit memory (Bremner et al., 1995c). Serotonin is likely involved in the effect of stress on the hippocampus because it is involved in both learning and memory and in stress and anxiety. The under-activation of serotonin neurotransmitter systems has been implicated in anxiety disorders, and selective serotonin re-uptake inhibitors have become the primary treatment for anxiety disorders (Linthorst & Reul, 2008; Ressler & Nemeroff, 2000). Conversely, serotonin levels have been shown to rise in the hippocampus during stressful situations (Linthorst, Flachskamm, Barden, Holsboer, & Reul, 2000; Linthorst & Reul, 2008; Rueter & Jacobs, 1996). Based on these studies, in addition to other animal and human studies, it appears that serotonin plays a role in stress and anxiety; however, that role is still unclear (Buhot, 1997; Buhot, Martin, & Segu, 2000; Sirvio, Riekkinen, Jakala, & Riekkinen, 1994).

Impact of Psychological Trauma on Memory: PTSD as a Model

Patients with PNES demonstrate a variety of cognitive impairments, most notably deficits in memory functioning. However, the reasons for these impairments are still largely unexplained. Studies in patients with posttraumatic stress disorder (PTSD) offer insight into a population that has both memory impairments and a history of psychological trauma. As such, PTSD serves as a potential model for understanding memory impairment in PNES patients. This model will assist in the examination of the effect of psychological trauma on the hippocampus, and resulting memory impairments in PTSD populations.

Overview of PTSD

PTSD is defined as the development of characteristic symptoms following exposure to an extreme traumatic stressor. Subsequent to surviving a traumatic event, the trauma is persistently re-experienced through recollections, dreams, acting or feeling as if it were recurring, or distress and psychological reactivity following exposure to cues resembling the event. The person demonstrates persistent avoidance of stimuli associated with the trauma, such as avoiding thoughts, feelings, or activities, and demonstrates a numbing of general responsiveness, such as feeling detachment from others. In addition, the person experiences unrelenting symptoms of increased arousal, such as hypervigilance, increased startle response, and/or difficulty concentrating (*Diagnostic and Statistical Manual of Mental Disorders*, 2000).

PTSD and Memory Functioning in Various Clinical Populations

Studies investigating memory functioning in PTSD have used a variety of patient groups including war veterans (generally Vietnam veterans), adults with a history of childhood abuse, rape survivors, children with PTSD, domestic violence survivors, Holocaust survivors, and groups with mixed etiology (all groups having a diagnosis of current or lifetime PTSD). Control groups have ranged from healthy non-traumatized controls, to those who experienced similar trauma but did not develop PTSD, such as combat veterans or rape survivors without PTSD. Study and control groups have generally been matched on various demographic variables, such as age, education, and gender. Studies have examined both verbal and nonverbal memory with measures such as the WMS-R and WMS-III memory subtests, CVLT, Rey Complex Figure Test (RCFT;

Rey, 1941), BVRT, Selective Reminding Test, Rey AVLT, Continuous Visual Memory Test (CVMT; Trahan & Larrabee, 1988), and the Benton Visual Form Discrimination (Campo & Morales, 2003).

Vietnam veterans.

Studies of memory functioning in Vietnam veterans with PTSD have indicated both verbal and nonverbal memory deficits. Bremner et al. (1993) compared 26 Vietnam veterans with PTSD (psychiatric inpatients) to 15 normal controls using the WMS-R and the Selective Reminding Test. Patients with a history of traumatic brain injury, neurological disorder, current alcohol abuse, or psychosis were excluded from the study, and alcohol and drug abuse were monitored for two months prior to the study. The authors reported that PTSD patients had significantly lower immediate and delayed recall scores on the Logical Memory section of the WMS-R than the normal controls. Additionally, PTSD patients scored significantly lower than control subjects on most of the measures for the visual and verbal components of the Selective Reminding Test, suggesting deficits in both initial learning and delayed recall for both verbal and visual material. The authors indicated that the PTSD group had a 67% retention rate on the Logical Memory component of the WMS-R, which is comparable to the 53-74% retention rates in patients with TLE, a population with clearly documented temporal lobe damage and hippocampal involvement (Bremner et al., 1993). Gilbertson, Gurvits, Lasko, Orr, & Pitman (2001) reported similar results when comparing Vietnam veterans with PTSD (psychiatric outpatients) to a control group of veterans without PTSD using the WMS-R and the RCFT. In this study, veterans with past, but not current PTSD were

excluded, as well as subjects with positive neurological histories (e.g. brain tumor and traumatic brain injury). They also reported that mean memory performance for the PTSD patients was well within normal limits, suggesting relative impairment rather than true impairment. It is important to note that the authors attributed the differences on the WMS-R between the two groups to above-average performance in the non-PTSD control group (scores were generally in the high average range as compared to test norms), rather than impaired performance in the PTSD group (scores were generally in the average range compared to test norms; Gilbertson et al., 2001). These results might suggest that above average memory functioning may serve as a protective factor against developing PTSD. However, premorbid functioning in both groups is unknown, and because the PTSD patients had significantly more combat exposure than non-PTSD patients, it is difficult to determine whether above average functioning is a protective factor or if PTSD leads to reduced memory performance.

Studies utilizing the CVLT and Rey AVLT as measures of verbal memory reported deficits in memory similar to studies using the WMS-R (Barrett, Green, Morris, Giles, & Croft, 1996; Vasterling, Brailey, Constans, & Sutker, 1998; Vasterling et al., 2002; Yehuda, Keefe et al., 1995). However, these studies have several limitations. For example, several studies found significant differences between the PTSD and control groups on only one score of the CVLT (e.g. immediate recall or retroactive interference) and often the difference in raw scores between groups was so small (e.g. one point) that the clinical relevance of the finding is unclear. Vasterling et al. (2002) also reported significantly greater deficits in nonverbal memory in the PTSD group as measured by the CVMT, and Sachinvala, Kling, Suffin, Lake, and Cohen (2000) reported both verbal and

nonverbal memory deficits as measured by the Cognitive Evaluation Protocol (McGuire et al., 2000), a touch screen computerized test of memory functioning.

Former POW's and Holocaust survivors.

The finding of decreased memory functioning in Vietnam veterans has been replicated among former prisoners of war (POW) and Holocaust survivors. POW survivors from the Korean Conflict had a higher prevalence of PTSD as compared with other combat veterans who had not been POW's and also performed more poorly on the verbal and nonverbal subtests of the WMS (Sutker, Winstead, Galina, & Allain, 1991). However, the study did not use a normal control group or report raw or scaled score means; so it is difficult to know if the difference between groups is clinically significant or if the POW group is impaired in comparison to population norms. Similarly, Holocaust survivors with PTSD performed more poorly on Paired-Associate Recall and the CVLT as compared to Holocaust survivors without PTSD and normal control subjects (Golier et al., 2002; Yehuda, Golier, Halligan, & Harvey, 2004; Yehuda et al., 2005). In these studies, patients were compared to normal controls, and Golier et al. (2002) reported that 12.9% of PTSD patients were impaired in relation to the non-PTSD group, and 35.5% of the PTSD group were impaired in relation to the normal (non-exposed) control group. However, it is important to note that the PTSD group had significantly lower IQs, as well as significantly less education, which may have impacted their scores on memory measures.

Survivors of child abuse, rape, and female genital mutilation.

Other trauma victim populations, including survivors of rape, childhood abuse, and female genital mutilation have also appeared to demonstrate memory deficits when compared to trauma-exposed subjects without PTSD and non-exposed controls. Female survivors of childhood sexual abuse with PTSD performed more poorly on verbal memory measures of the WMS-R compared to survivors without PTSD and normal controls (Bremner, Vermetten, Afzal, & Vythilingam, 2004). In general, despite the lack of statistical analysis, it appears that, in this study, abused subjects with PTSD performed more poorly than abused subjects without PTSD, and abused subjects without PTSD performed more poorly than non-abused controls. Bremner et al. (1995b) also reported that verbal memory deficits, as measured by the WMS, were associated with the severity of childhood abuse in PTSD patients. Based on these results, it is possible that the severity of the traumatic stress experienced may correlate with memory functioning, such that severe stress (e.g. stress that leads to PTSD development) results in more profound memory deficits than stress that is less severe. Rape victims with PTSD performed more poorly on the delayed free recall index of the CVLT than rape victims without PTSD and non-traumatized control subjects (Jenkins, Langlais, Delis, & Cohen, 1998). Furthermore, this study reported performance in comparison to normative standards for age and education and indicated that one third of the PTSD-positive group fell at least two standard deviations below the mean for delayed free recall while fewer than 5% of the other two groups were this impaired. This indicates that the memory deficits in many of the patients with PTSD may be classified as a significant impairment in memory functioning. Finally, survivors of female genital mutilation, as compared with

uncircumcised women, showed a higher rate of PTSD, as well as a higher rate of immediate and delayed nonverbal memory impairment, as measured by the RCFT (Behrendt & Moritz, 2005). While this is one of the few studies reporting significant differences in nonverbal memory deficits between PTSD and exposed non-PTSD patients, they did not report mean raw or normed scores; so it is again difficult to know if these differences are clinically relevant or represent significant impairment.

Mixed trauma etiology.

The finding of memory impairment in PTSD patients was also noted in populations with mixed trauma etiology who were admitted to a hospital center for traumatic injuries. The traumatic incidents included: motor vehicle and industrial accidents, and impersonal assaults (e.g. nonsexual or perpetrator not known to the victim). The patients were screened and eliminated if they had impairment on the Galveston Orientation and Amnesia Test (Levin, O'Donnell, & Grossman, 1979), post-concussive symptomatology, or the presence of a psychiatric disorder in the six months prior to the accident. Immediately (1-2 days following medical stabilization) after the accident (baseline), patients were evaluated for PTSD severity and were also given neuropsychological evaluations. Six weeks later (follow-up) the patients were again assessed for the presence of PTSD or other psychiatric disorders, and 21% of patients had developed PTSD in the six weeks following the accident. None of the memory measures correlated significantly with PTSD severity at baseline, but there were significant negative correlations between follow-up PTSD severity and two verbal memory scales on the Rey AVLT: the delayed recall score and the retroactive interference score (both of

which were administered at baseline). While these findings suggest that patients with memory deficits immediately following an accident may be at greater risk for developing PTSD, it is unclear whether these deficits existed prior to the accident or developed as a result of the accident (Bustamante, Mellman, David, & Fins, 2001). Additionally, children ages 11-17 with current PTSD resulting from road traffic or personal violence incidents performed significantly worse than normal controls on the Rivermead Behavioural Memory Test (Wilson, Cockburn, Baddeley, & Hiorns, 1989). According to published norms, 55.6% of child and adolescent PTSD patients suffered from poor memory and 22.2% had impaired memory. In contrast, only 13.6% of normal controls had poor memory and none had impaired memory (Moradi, Doost, Taghavi, Yule, & Dalgleish, 1999). The above results suggest that, similar to adults with PTSD, a large proportion of children with PTSD also suffer from memory impairment compared to normal controls and published norms.

Reasons for Memory Impairment

In conclusion, while there are inconsistencies in the literature, there is a general pattern suggesting that PTSD is associated with memory deficits across populations subjected to various types of trauma. It is important to note that while a few studies compared memory functioning amongst subjects with PTSD, subjects without PTSD who had experienced similar types of trauma, and normal controls, there are various limitations to these studies, and the majority of studies do not make this comparison. Therefore, it is difficult to determine whether subjects who experience trauma but do not

develop PTSD also exhibit memory deficits. As such, the impact of trauma on memory functioning, independent from PTSD should be further explored.

Another factor that deserves additional investigation is whether trauma that occurs during childhood has a greater impact on memory functioning then trauma that occurs as an adult. Childhood trauma occurs while the brain is in early stages of development and as a result, could potentially lead to greater memory impairments.

Several hypotheses have been put forth with regard to the cause of memory impairments in PTSD patients. Some authors suggest memory impairment may be a preexisting risk factor for developing PTSD (Vasterling et al., 2002). However, other studies suggest that memory impairment may develop following a traumatic event and the development of PTSD (Bustamante et al., 2001). The known role of the hippocampus in memory functioning, along with stress induced hippocampal damage and memory impairment seen in animal models, support the idea that decreased memory functioning in PTSD may be related to medial temporal lobe and hippocampal dysfunction.

The Hippocampus and Memory in PTSD

Studies in humans measuring hippocampal volume have investigated the relationship between this variable and memory impairment in PTSD.

Hippocampal Volume and PTSD

Two studies reported that survivors of physical and sexual abuse, with current PTSD, have a smaller left hippocampal volume than non-traumatized controls. Differences in left hippocampal volume between PTSD patients and normal controls

ranged from 5-12%. Patients also performed more poorly than normal controls on several verbal measures of memory, but scores on these measures were not correlated with hippocampal volume (Bremner et al., 1997; Stein, Koverola, Hanna, Torchia, & McClarty, 1997). In Vietnam combat veterans with PTSD, magnetic resonance imaging (MRI) hippocampal volume was 8% smaller on the right side as compared with controls matched for age, demographic characteristics, and alcohol abuse history (Bremner et al., 1995a). While another study of 10 combat related PTSD patients failed to find hippocampal volumetric differences, they reported that 50% of PTSD patients had a cleft in the callosal-septal interface. The authors suggested that it is tempting to interpret this finding as evidence for an anatomical change that preceded the development of PTSD, and as a result they hypothesize that the cleft is a physiological marker of vulnerability to PTSD following stress (Myslobodsky et al., 1995). However, they were unable to provide proof of this relationship, and they also offered no evidence that this abnormality did not follow the development of PTSD. Finally, small sample size may account for the lack of volumetric differences in this study.

Four studies reported decreased volume in both right and left hippocampi. Gurvits et al. (1996) compared seven Vietnam combat veterans with PTSD to seven Vietnam veterans without PTSD and reported significantly reduced right and left hippocampi in PTSD veterans. These results held true after adjusting for age, total brain volume, and alcohol abuse history. Hippocampal volume was correlated with only one measure of memory, which the authors suggested might have been a result of small sample size (Gurvits et al., 1996). Similar results were reported for adult survivors of

childhood sexual abuse. PTSD patients showed a 16% smaller hippocampal volume than abused patients without PTSD and a 19% smaller volume than non-traumatized controls (Bremner et al., 2003). No statistical comparison was made between abused patients without PTSD and non-traumatized controls. Despite the omission of this latter comparison, there seems to be an apparent tendency towards a progressive reduction in hippocampal volume that is inversely correlated with level of traumatic experience and subsequent psychological response to trauma. These data also support those studies reporting a positive correlation between PTSD severity and the severity of memory deficits (Bremner et al., 1995b; Bremner et al., 2004). Finally, two studies compared Dutch police officers with PTSD to non-traumatized police officers without PTSD and reported significantly smaller right and left hippocampal volume for PTSD patients (10.6% total reduction, 12.6% reduction of left hippocampus). In addition, they reported increased cortisol levels and more perseverations on the CVLT in PTSD patients as compared to control subjects (Lindauer, Olff, van Meijel, Carlier, & Gersons, 2006; Lindauer et al., 2004).

In contrast to the studies discussed above, several other studies reported no difference in hippocampal volume between PTSD patients with a history of abuse and both non-abused control subjects and abused control subjects without PTSD. Pederson et al. (2004) was unable to replicate findings in PTSD patients with a history of childhood abuse using a sample size of 17 subjects in each group. The authors cited younger age (20 years on average) and milder PTSD symptoms as possible reasons for these findings. Golier et al. (2005) reported no differences in hippocampal volume between Holocaust

survivors with and without PTSD despite findings of poorer memory performance on several verbal measures of memory in the PTSD patients. However, subjects in this study were significantly older than subjects in most other studies. Since there is evidence of age-related reduction in hippocampal volume in association with memory impairment in normal aging (De Leon et al., 1997; Golomb et al., 1993; Golomb et al., 1994), the effects of normal aging could have obscured the effects due to PTSD. De Bellis et al. (1999b) reported no difference between hippocampal volume in 44 maltreated children and adolescents with PTSD and 61 matched non-abused controls. When considering these findings, it is important to note that this is the only study at the time of the current literature review that utilized children and adolescents. Hippocampal maturity was still occurring in these young subjects, which could mask the full effects of trauma on the hippocampus. Finally, a longitudinal study of 37 survivors of a traumatic event (recruited following admission to the emergency room), who met criteria for PTSD, were given an MRI one week and six months following the trauma. At the six month follow-up, 10 (27%) participants met PTSD criteria. The authors reported no reduction in hippocampal volume between baseline and follow-up and no differences between those with PTSD and those without PTSD at the six month follow-up (Bonne et al., 2001). However, it is possible that structural damage may only occur after prolonged trauma or prolonged symptoms of PTSD.

There is some evidence that suggests that both the memory deficits and the decreases in hippocampal volume associated with PTSD may be reversible. Vermetten, Vythilingam, Southwick, Charney, & Bremner (2003) reported that after treatment with

the SSRI paroxetine for 36-48 weeks, patients with PTSD showed a 4.6% mean hippocampal volume increase as measured by MRI and a significant improvement in verbal declarative memory functioning as measured by the WMS-R and the Selective Reminding Test. Additionally, Bremner et al. (2005) reported that PTSD patients showed a 5% increase in right hippocampal volume after three months of treatment with phenytoin.

Functional Neuroimaging of the Hippocampus

Studies utilizing functional neuroimaging of the hippocampus are limited, and findings are fairly inconsistent. Bremner et al. (2003) used positron emission tomography (PET) scans with $[^{15}O]H_2O$ to assess hippocampal activation during a verbal memory encoding task. In addition to the volumetric findings reported above, patients with PTSD demonstrated no significant left hippocampal activation as compared to traumatized patients without PTSD and non-traumatized controls (Bremner et al., 2003). Additionally, studies using magnetic resonance spectroscopy (MRS) have reported decreased N-acetyl-L-aspartic acid (NAA; an indicator of neuronal density) in the hippocampus of patients with chronic PTSD, which may indicate loss of neuronal integrity. These findings were replicated in POW survivors and Vietnam veterans with PTSD as compared to POW survivors and Vietnam veterans without PTSD, as well as compared to non-combat exposed controls (S. Brown, Freeman, Kimbrell, Cardwell, & Komoroski, 2003; Freeman, Cardwell, Karson, & Komoroski, 1998; Mohanakrishnan Menon, Nasrallah, Lyons, Scott, & Liberto, 2003; Schuff et al., 2001; Villarreal et al., 2002). In a study using PET scans, firefighters with PTSD had smaller increases in

regional cerebral blood flow (rCBF) during a word stem completion (high vs. low recall) task than firefighters without PTSD. However, this difference was accounted for by a greater hippocampal rCBF at baseline. When high and low recall conditions of the word stem completion task were collapsed, the PTSD group had higher rCBF in the hippocampus. In addition, the severity of PTSD symptoms was positively correlated with rCBF in the hippocampus and parahippocampal gyrus. They also reported smaller hippocampal volumes in the PTSD patients and speculated that the increased rCBF may indicate reduced efficiency of the hippocampus (Shin et al., 2004). Another study using single photon emission computed tomography (SPECT) reported that at baseline, PTSD patients, as compared to normal controls, showed increased regional blood flow in the hippocampal regions (Sachinvala et al., 2000).

Reasons for Hippocampal Volume Reduction

In summary, these findings suggest that patients with PTSD have decreases in hippocampal volume. There are several explanations for the smaller hippocampal volume in PTSD. Some propose that reduced hippocampal volume may be a preexisting risk factor for developing PTSD after exposure to a trauma. Gilbertson et al. (2002) provides support for this theory, reporting that both combat related PTSD patients and their non-trauma exposed identical twins showed similar smaller hippocampal volumes as compared to both Vietnam veterans without PTSD and their non-combat exposed identical twins. An alternate explanation for the findings of reduced hippocampal volume in PTSD is that traumatic events and resulting PTSD may cause a reduction in hippocampal volume. This explanation proposes that extreme stress experienced during

and after the traumatic event may lead to changes, such as elevated glucocorticoid levels in the hypothalamic pituitary adrenal (HPA) axis, that have a neurotoxic effect and damage the hippocampus. Support for this theory is provided below.

Stress, Glucocorticoids, and the HPA Axis in Memory Impairment

Stress and the HPA Axis

The HPA axis is activated when homeostasis is disrupted (this is referred to as stress). During a stress response, a cascade of events takes place beginning with the release of corticotrophin releasing factor (CRF) from the hypothalamus, followed by the release of adrenocorticotropin hormone (ACTH) from the pituitary to the blood stream, which in turn results in release of glucocorticoids (cortisol in humans and corticosterone in rats) from the adrenal cortex. The activation of the HPA axis is generally the body's adaptive response to stress and mobilizes the body for action, but prolonged activation can cause health risks (Lupien et al., 2005).

The hippocampus has a high concentration of glucocorticoid receptors (McEwen, 1998; McEwen, De Kloet, & Rostene, 1986). There are two receptor subtypes for glucocorticoids (MR and GR). de Kloet, Oitzl, & Joels (1999) propose that cognitive function is best explained by the differential effects of activation of the two receptors within the hippocampus and frontal lobes. MRs play a role in behavioral reactivity during novel situations, and GRs, are involved in consolidation of learned information (de Kloet et al., 1999; Oitzl & de Kloet, 1992; Roozendaal & McGaugh, 1997).

Glucocorticoids and Memory Functioning

Repeated, prolonged exposure to stress through severe emotional trauma leads to increases of glucocorticoids and enkephalins that damage hippocampal pyramidal neurons, affecting the functioning of the hippocampus (Joseph, 1999; McEwen, 1998; Weber & Reynolds, 2004). Stress-induced hippocampal dysfunction leading to memory impairment occurs in a two-fold process. Initially, acute stress increases cortisol secretion, which disrupts functions in the hippocampus and temporal lobe that are involved in short-term memory processes (McEwen et al., 1995a; McEwen & Sapolsky, 1995b). This short-term impairment is reversible and short-lived (Lupien & McEwen, 1997). However, repeated stress can lead to atrophy of the pyramidal neurons in the CA3 region of the hippocampus. The release of both glucocorticoids and excitatory amino acid neurotransmitters during and after stress, contribute to hippocampal atrophy. Atrophy resulting from short-term stress is generally reversible, but during prolonged, chronic stress, hippocampal neurons may begin to die (Uno, Tarara, Else, Suleman, & Sapolsky, 1989). This atrophy can lead to cognitive impairments involving declarative memory (McEwen & Sapolsky, 1995b)

Cortisol and PTSD

Despite the knowledge that stress can increase glucocorticoid secretion leading to hippocampal damage and memory impairments, studies examining cortisol levels in PTSD have been inconclusive. Some studies have reported hypersecretion of cortisol in patients with current PTSD (Davidson & Baum, 1986; De Bellis et al., 1999a; Lemieux & Coe, 1995; Lindauer et al., 2006; Pitman & Orr, 1990), which is consistent with

theories of increased cortisol leading to hippocampal damage and memory deficits. However, other studies have reported normal levels of glucocorticoids (Baker et al., 1999) or lower than normal levels of glucocorticoids in patients with PTSD as compared with normal controls (Mason, Giller, Kosten, Ostroff, & Podd, 1986; Yehuda, Boisoneau, Lowy, & Giller, 1995; Yehuda, Kahana et al., 1995; Yehuda et al., 1990). One explanation posed for the inconsistent levels of glucocorticoids found in PTSD is that high levels of cortisol at the time of the stressor may lead to adaptation and long-term changes in cortisol regulation, eventually leading to decreased cortisol in the chronic stages of the disorder (Putnam & Trickett, 1997). Findings of enhanced dexamethasone suppression and increased glucocorticoid receptors without differences in cortisol levels in patients with PTSD support this hypothesis of a negative feedback sensitivity (Stein, Yehuda, Koverola, & Hanna, 1997; Yehuda, Lowy, Southwick, Shaffer, & Giller, 1991). The neuroendocrine alterations associated with PTSD, such as low cortisol levels, increased sensitivity, and greater glucocorticoid receptor numbers, are different from other stress responses. Hippocampal atrophy reported by many studies may be a result of increased glucocorticoid receptor sensitivity rather than increased levels of cortisol (Yehuda, Giller, Southwick, Lowy, & Mason, 1991; Yehuda, Lowy et al., 1991).

Stress and Memory Functioning in Animals

While studies of the effects of cortisol on the hippocampus in PTSD patients are somewhat inconclusive, studies in animals have provided a more solid link between stress, levels of cortisol in the brain, and hippocampal damage. Inescapable stress in animals provides indirect evidence of this link. For example, studies utilizing footshock

or forced swim resulted in learning deficits as measured by impairments in maze escape behaviors in the rat (Drugan, Ryan, Minor, & Maier, 1984; Seligman & Maier, 1967; Sherman, Sacquitne, & Petty, 1982). Direct glucocorticoid exposure has been shown to result in decreased dendritic branching (Sapolsky, Packan, & Vale, 1988; Watanabe, Gould, & McEwen, 1992; Woolley, Gould, & McEwen, 1990), alterations in the synaptic terminal (Magarinos, Verdugo, & McEwen, 1997), loss of neurons (Uno et al., 1990), and inhibition of neuronal regeneration (Gould, Tanapat, McEwen, Flugge, & Fuchs, 1998) in the CA3 region of the hippocampus. In monkeys subjected to severe stress, high levels of glucocorticoids released during stress were associated with damage to the CA3 region of the hippocampus (Sapolsky, 1996b; Sapolsky et al., 1988; Sapolsky, Uno, Rebert, & Finch, 1990; Uno et al., 1989), and this type of damage is associated with memory deficits (Arbel, Kadar, Silbermann, & Levy, 1994; Luine, 1994; Sapolsky, 2000; Watanabe et al., 1992). Additionally, subcutaneously implanted pellets that provide sustained release of glucocorticoids and mimic chronic stress situations led to deficits in learning and memory for maze escape behaviors (Arbel et al., 1994). Both cortisol treatment and chronic psychosocial stress for 15 weeks in the tree shrew resulted in impaired hippocampus mediated memory and showed a trend toward hippocampal volume reduction (Ohl, Michaelis, Vollmann-Honsdorf, Kirschbaum, & Fuchs, 2000).

Stress and Memory Functioning in Humans

Human studies of stress, glucocorticoids, and memory functioning have yielded similar results. Vasterling et al. (2006) reported that in a study of 961 active-duty army soldiers who were given baseline (before deployment to Iraq) and follow-up (mean of 73

days after deployment) neuropsychological measures, deployed soldiers showed decreases in verbal learning and visual-spatial memory at follow-up. Furthermore, deployment was associated with increases in tension as measured by the Profile of Mood States (McNair, Lorr, & Droppelman, 1971). The authors proposed that stress symptoms were one factor that was associated with reduced memory functioning following deployment (Vasterling et al., 2006).

Studies that have examined the relationship between glucocorticoids and memory functioning support the findings by Vasterling et al. (2006). Increases in both endogenous and exogenous glucocorticoids were associated with reductions in memory performance. Higher levels of baseline and stress-induced endogenous cortisol appear to be associated with poorer memory performance. For example, a longitudinal study of older men and women measured levels of endogenous cortisol and memory performance at baseline and 2.5 years later at follow-up. Results suggested that higher levels of cortisol at baseline were associated with poorer memory performance in women ages 70-79, and women who continued to exhibit increases in cortisol at follow-up were more likely to show declines in memory performance (Seeman, McEwen, Singer, Albert, & Rowe, 1997). Additionally, when cortisol levels declined, an improvement in memory function was observed (Seeman et al., 1997; Wolkowitz et al., 1997). Stress induced cortisol increases also appear to be associated with decreases in memory performance. For example, in healthy subjects, cortisol increases during a stress test were negatively correlated with memory functioning (Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996; Lupien & McEwen, 1997). Patients with Cushing's disease, a disease that involves

excessive release of cortisol over long periods of time, have deficits in verbal declarative memory that were correlated with hippocampal volume reduction (Starkman, Gebarski, Berent, & Schteingart, 1992). Administration of exogenous glucocorticoids, dexamethasone, or cortisol also resulted in verbal declarative memory impairments in healthy humans (Keenan, Jacobson, Soleymani, & Newcomer, 1995; Kirschbaum et al., 1996; Newcomer, Craft, Hershey, Askins, & Bardgett, 1994; Wolkowitz et al., 1990). For example, healthy subjects who received exogenously administered cortisol had deficits in memory performance as compared to subjects who were not given exogenous cortisol (Kirschbaum et al., 1996; Lupien & McEwen, 1997). Taken together, these findings suggest that the increases in glucocorticoids released during stress have direct but potentially reversible effects on memory, and these effects are mediated through the hippocampus (Bremner, 1999).

Study Aim and Hypotheses

In summary, it is clear that glucocorticoids released during stress can have an effect on the hippocampus. However, it is unclear whether the stress that results from psychological trauma accounts for the memory deficits seen in PNES patients. The first aim of this study was to confirm previous studies comparing ES patients to PNES patients on measures of memory functioning. This study utilized stringent inclusion criteria, which provided a rather homogeneous sample. Patients with comorbid ES and PNES were eliminated from the study; many previous studies have included these patients, which potentially created a major confound. This study also controlled for depression, anxiety, and poor effort, which, to date, has not been done. Finally, it has one

of the largest sample sizes with only two prior studies reporting larger samples. A TLE control group was utilized as a disease control group. The second aim of this study was to determine whether trauma is a contributing factor to the memory impairment in PNES populations. Finally, it aimed to explore the impact of trauma on memory functioning while controlling for PTSD.

Based on the results from the existing literature, it was hypothesized that there would be no difference between TLE and PNES groups on verbal and non-verbal measures of memory. It was also hypothesized that PNES patients with a history of psychological trauma would be significantly more impaired on memory measures than PNES patients without a history of trauma. Since PNES patients have a particularly high incidence of sexual abuse as compared with other types of trauma, this study also explored whether subjects with a history of sexual abuse exhibit a greater degree of memory impairment, which could potentially explain the memory deficits seen in PNES populations. As a result, it was hypothesized that PNES patients with a history of sexual abuse would have significantly more impaired memory measures than PNES patients with other types of trauma and PNES patients with no history of psychological trauma. Additionally, it was hypothesized that PNES patients with a history of childhood abuse would show significantly more impairment on memory measures than PNES patients with adult trauma or PNES patients with no trauma. Finally, this study aimed to assess the degree of impairment in both PNES and ES subjects as compared to population norms. It was hypothesized that both groups would be in the impaired range on all four measures of memory in relation published norms.

METHODS

Participants

One hundred and ten patients who met the study criteria were selected from the New York University Comprehensive Epilepsy Center (CEC) from 2000-2007. Participants in the PNES group were selected from consecutive admissions and participants in the TLE group were selected from an existing database. Medical and neuropsychological data was obtained from patient charts. All participants underwent psychological and neuropsychological evaluations during their video-EEG (V/EEG) monitoring admission. Participants included 90 female and 20 male subjects and ranged in age from 18-60 years old. The demographic characteristics of the study population are summarized in Tables 1 and 2. Fifty-five patients with PNES were compared with a control group of 55 patients with TLE. PNES patients also underwent psychiatric evaluations during their V/EEG monitoring admission. There was an equal ratio of male and female participants in each group. All diagnoses were established using V/EEG monitoring during their inpatient admission. For patients to be given a diagnosis of PNES, they had to experience what they reported to be a "typical seizure," with no ictal EEG discharges observed on the EEG recording at the time of their seizure. Additionally, all other physiological causes for the seizure were ruled-out. Patients were given a diagnosis of TLE if they experienced a "typical seizure" correlated with EEG seizure activity originating from and confined to the temporal lobe. Within the TLE group, there were 20 (36.4%) participants with Right TLE (RTLE) and 35 (63.6%) participants with Left TLE (LTLE).

Patients in the two groups were matched on age, education, and gender (see Table 1). Patients with comorbid PNES and ES were excluded from the study. Patients with an IQ below 70, as measured by the Weschler Adult Intelligence Scale –Revised (WAIS-R; Wechsler, 1981) or the Weschler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997a), were excluded from the study. Patients were also excluded if they had experienced a head trauma with loss of consciousness greater than 60 minutes, or if they had experienced any other major brain trauma, disease, or infection. Patients with current substance abuse disorders were excluded from the study. Finally, within the TLE group, patients with a history of status epilepticus were excluded because of the potential for severe brain damage.

Psychological Assessments

Psychological trauma histories were obtained from all PNES subjects by the CEC neuropsychiatrist, Kenneth Alper M.D., in the context of a psychiatric interview that closely modeled the Structured Clinical Interview (SCID), for the DSM III-R or DSM IV (First, Spitzer, Gibbon, & Williams, 1997; Spitzer, Williams, Gibbon, & First, 1990). The interview also included abuse and trauma history (Alper et al., 1993). This included childhood or adult physical or sexual abuse, or other trauma (e.g. combat exposure, kidnapping, witness to a violent crime). Patients were asked if they had ever been physically or sexually abused. Childhood abuse was defined as abuse occurring when the victim was 18 years old or younger. Most patients volunteered abuse histories simply in response to this question. However, if the patient denied a history of abuse, their response was followed by specific questions as to whether the patient had ever been,

"approached sexually by anyone at age 14 or younger or in any manner suggestive of physical coercion or implicit or explicit threats of violence at any age (Alper et al., 1993, p. 43)." Generally, the involvement of a household or family member or the use of coercion clearly distinguished abuse from normal adolescent sexual exploration. If the sexual activity did not involve coercion or a household member and occurred before the age of 14, it was determined to be indicative of abuse if the perpetrator was at least 5 years older than the patient. The type of sexual activity that took place was assessed, and abuse was defined as a purposeful attempt at sexual contact by the perpetrator. "Purposeful" was defined as actions that would directly result in sexual contact with the victim if they were to go unopposed. Adult sexual abuse was defined as unwanted sexual contact by the perpetrator occurring either when the patient was unable to defend him or herself or with the use of coercion such as the use of threat, physical assault, or a weapon.

Childhood physical abuse was defined as, "violence deliberately inflicted on a patient during childhood in a context in which the patient was unable to actively defend himself or herself by virtue of the physical advantage or parental authority of the perpetrator (Alper et al., 1993, p. 43)." Adult physical abuse was defined as deliberately inflicted violence on a patient when the patient was unable to actively defend him or herself due to the physical advantage of the perpetrator, the use of threat, or the use of a weapon. Sexual abuse was coded on sexual invasiveness and physical abuse was coded on severity (Alper et al., 1993). Refer to Table 3 for coding of physical and sexual abuse.

Eight participants were determined to have experienced trauma that did not fall under the category of physical or sexual abuse. These participants had been exposed to

several types of specific traumatic events (e.g., combat and gang violence, witnessing the death of others, carjacking, attempted murder, and/or witnessing the repeated abuse of a sibling as a child). The "other trauma" category did not include reported emotional abuse as this is often quite subjective and difficult to define.

Approximately 50% of PNES patients experienced some form of trauma. Trauma prevalence frequencies for PNES subjects are reported in Table 4. Abuse severity frequencies for PNES subjects are reported in Table 5.

A diagnosis of PTSD was also made for each of the participants during their psychiatric interview. Patients were diagnosed with PTSD if they met DSM III-R or DSM IV criteria. PTSD diagnosis was categorized according to current diagnosis, past diagnosis, or rule out diagnosis. See Table 6 for PTSD frequencies in the study population.

Materials

Neuropsychological Assessments

Memory was evaluated using the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987) and the Rey- Osterrieth Complex Figure Test (RCFT; Osterrieth, 1944; Rey, 1941). The CVLT is a list learning task wherein participants are read a list of 16 words (list A) and asked to repeat as many words as they can remember. This list is repeated over five successive learning trials, and participants are asked to repeat as many words as possible after each successive trial. The total number of words recalled from the five trials becomes the Total Learning score. Following a single

attempt to learn an interference list of 16 new words (list B), the ability to immediately recall the previously learned words (list A), with and without being cued, is assessed. After a 20-minute delay during which unrelated nonverbal tasks are performed, the ability to recall (with and without being cued) and recognize the words is again tested. Long Delay Free Recall (LDFR) is the total number of words recalled following the delay without being cued. The recognition trial consists of the 16 target items from list A, which are randomly combined with 16 distractor words. Participants respond "yes" if the word was from list A and "no" if it was not. Level of performance is determined by the number of correct hits and false-positive errors. From this, the Discriminability Index can be calculated, which is the ability to distinguish list A words from the distractor words. It is calculated by the absolute difference of standard deviation between the hit rate and false-positive rate. Discriminability is considered one of the best measures of recognition memory because it takes into account response bias. The main variables of interest for the present study included: Total Learning, LDFR, and Discriminability (note that two participants from the PNES group were missing Discriminability scores because the recognition trial could not be administered).

The RCFT is a task in which a complex figure is presented and the subject is required to copy the figure (Copy Trial). It is then removed, and following a 20–30 minute delay, a recall trial is administered wherein the participant is asked to draw the figure from memory (Delay Trial). The scores for both the Copy and Delay Trials are derived from the accuracy and placement of the various components of the figure. The main variable of interest for the present study was the Delay Trial.

Self-Report Measures

Subjective memory was evaluated using an altered version of Green and Allen's (1997) Memory Complaints Inventory (MCI) that was adjusted for use with an epilepsy population. The MCI assesses patients' self-perceptions of memory functioning. The MCI is a 65-item self-administered questionnaire designed to quantify self-perceptions of memory. It has a total score indicating global assessment of memory self-perception, which is the variable of interest for the present study.

Depression and anxiety were evaluated using the Beck Depression Inventory (BDI; A. T. Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) or the Beck Depression Inventory-II (BDI-II; A.T. Beck, Steer, & Brown, 1996), and the Beck Anxiety Inventory (BAI; A. T. Beck, Epstein, Brown, & Steer, 1988). The BDI and BDI-II are 21 item self-report rating inventories measuring characteristic attitudes and symptoms of depression. They are rated on a scale of 0 to 3, with 3 being more severe. For the BDI, minimal depression is characterized by a total score of 0-9, mild is 10-19, moderate is 19-29, and any score above 29 is characterized as severe. For the BDI-II, minimal depression is characterized by a total score of 0-13, mild is 14-19, moderate is 20-28, and scores above 28 are characterized as severe. The BAI consists of 21 items also rated on a scale from 0 to 3. Each item is descriptive of affective, somatic, or panic-related symptoms of anxiety. For the BAI, minimal anxiety is characterized by a score of 0-7, mild is 8-15, moderate is 16-25, and any score above 25 is characterized as severe. In addition to the BDI and BDI-II, depression was evaluated using the depression scale from the Minnesota Multiphasic Personality Inventory-2 (MMPI-2; Butcher et al., 1989). The MMPI-2 is a

questionnaire used to identify personality structure and psychopathology. It consists of 567 items in a true/false format. For each of the scales, T scores over 65 are considered to be a clinical elevation. The depression scale consists of 57 items that reflect feelings of discouragement, pessimism, and hopelessness. For the purposes of this study, participants were considered to have anxiety if they scored above 7 on the BAI. Participants were considered to have depression if they scored above 13 on the BDI or BDI-II and they had a T score above 65 on the MMPI-II depression scale. If both depression measures were not available, the cutoff criterion was determined by either the BDI score or the MMPI-II depression T score. Not all participants were administered all of the depression and anxiety measures. Sixty-two participants were given the BAI, 63 were given the BDI or BDI-II, and 75 were given the MMPI-II.

Effort Measures

Effort was assessed using the Test of Memory Malingering (TOMM; Tombaugh, 1996), CVLT Hits (Curtis, Greve, Bianchini, & Brennan, 2006; Millis & Ricker, 1995; Trueblood, 1994; Trueblood & Schmidt, 1993), reliable digits from the WAIS-R/III Digit Span subtest (Iverson & Franzen, 1994, 1996; Iverson & Tulsky, 2003), and the Vocabulary scaled score minus the Digit Span scaled score from the WAIS-R/III (Iverson & Tulsky, 2003; Mittenberg, Theroux-Fichera, Zielinski, & Heilbronner, 1995). The TOMM is a visual recognition test that is designed to help distinguish malingers from people with true memory impairment. It is presented over two trials. During each trial, subjects are presented with 50 target pictures of common objects for 3-4 seconds each during a learning trial. They are then shown 50 recognition cards each containing two

pictures, one that was part of the target group and a second, novel picture. Subjects are asked to select the target picture that was presented during the learning trial. Norms are based on both cognitively intact samples and clinical samples. A score of 45 or greater on trial 2 is the recommended cutoff; scores lower than 45 are considered to be indicative of poor effort. For CVLT Hits (recognition trial), a score of less than or equal to 10 suggests insufficient effort (Ashendorf, O'Bryant, & McCaffrey, 2003; Curtis et al., 2006; Sweet et al., 2000). Reliable digits from the WAIS-R/III is calculated by the maximum reliable span forward and backward, in other words, the greatest number of digits recalled reliably forward and backward. A score of less than or equal to 6 is indicative of poor effort (Greiffenstein, Baker, & Gola, 1994; Greiffenstein, Gola, & Baker, 1995; Greve et al., 2007; Iverson & Tulsky, 2003; Mathias, Greve, Bianchini, Houston, & Crouch, 2002). Finally, Vocabulary minus Digit Span is calculated by subtracting the Digit Span subtest scaled score from Vocabulary subtest scaled score on the WAIS-R/III. Scores greater than or equal to 6 suggest poor effort on testing (Iverson & Tulsky, 2003; Miller, Ryan, Carruthers, & Cluff, 2004). For the purposes of this study, subjects were determined to have met the effort criteria if they either obtained a score of 45 or greater on Trial 2 of the TOMM (Tombaugh, 1996) or if they met the cutoff criteria on at least two of the three internal effort measures (CVLT hits, reliable digits, and Vocabulary minus Digit Span).

Procedure

Data for this retrospective study was compiled through a review of medical, psychiatric, and neuropsychological records. Patients with a diagnosis of PNES were

initially selected from psychiatric records. The TLE group was initially selected from an existing data set. Those who met the inclusion criteria discussed in the "Participants" section were included in the study. PNES and ES participants who failed the effort criteria were excluded from the study. Psychological trauma data was obtained through a review of psychiatric records and coded accordingly. A diagnosis of PTSD was also obtained through a review of psychiatric records, and participants were coded as having PTSD if they were given a current, past, or rule-out diagnosis. Medical data was acquired through a review of medical and neuropsychological charts. Neuropsychological and assessment data was obtained from records.

Memory was characterized using four dependent variables: CVLT Total Learning, CVLT LDFR, CVLT Discriminability, and RCFT Delay Trial.

Statistical Analysis

Preliminary Data Analysis

Ten of the participants from the PNES group were missing effort measures. To determine whether those participants should be included in the analysis, an independent samples two-tailed t-test was performed to assess whether there was a significant difference between the dependent variables for subjects who met the effort criteria and subjects who were missing effort measures.

To determine whether depression and anxiety needed to be controlled for in the study, two independent samples two-tailed t-tests were conducted using the depression and anxiety cutoffs discussed above. The first t-test utilized the combined sample (those

with PNES and TLE) and compared those with and without depression on all four dependent measures of memory. The second t-test also utilized the combined sample (those with PNES and TLE) and compared those with and without anxiety on the four dependent memory variables. Additionally, correlations were run between the dependent memory measures and continuous depression and anxiety scores from the BAI, BDI/BDI-II, and MMPI-II. To compare dependent memory measures between the PNES and TLE groups, an independent samples t-test was performed using the Bonferroni procedure to control for type I error rate (familywise error). It was important to consider the effect of the person's ability to copy the complex figure on their ability to accurately recall the figure after a delay. Poor copy scores will likely lead to poor delay scores and, as a result, the person's visual-spatial ability, rather than their non-verbal memory ability, is likely being measured. Controlling for the Copy Trial score helped to ensure that non-verbal memory was being assessed rather than visual-spatial ability. Therefore, a correlation was run to determine if the RCFT Copy Trial scores and the RCFT Delay Trial scores were correlated. Based upon the result of the previous correlation, an analysis of covariance (ANCOVA) was performed to assess whether there were differences in RCFT Delay Trial scores between the PNES group and the TLE group while controlling for RCFT Copy Trial scores.

Primary Data Analysis

To determine whether trauma was related to memory functioning in the PNES group, a 3-way analysis of variance (ANOVA) was performed comparing PNES patients with a history of trauma, PNES patients without a history of trauma, and TLE patients.

This was done for all four measures of memory. Next, a priori tests were executed comparing PNES patients with a history of trauma to PNES patients without a history of trauma and comparing PNES patients with a history of trauma to TLE patients. The ANOVAs were then repeated comparing PNES patients with a history of sexual abuse, PNES patients with a history of trauma other than sexual abuse, and PNES patients without a history of trauma. Finally, ANOVAs were used to compare PNES patients with a history of childhood abuse, PNES patients with a history of trauma other than childhood abuse, and PNES patients without a history of trauma. For the three analyses discussed above in which the RCFT Delay Trial score was the dependent variable, ANCOVAs were performed using the RCFT Copy Trial score as a covariate because of the relationship between the Copy Trial scores and the Delay Trial scores.

Secondary Data Analysis

To examine whether trauma was a predictor of memory impairment independent from PTSD, several planned comparisons were conducted. Two-tailed t-tests were performed comparing PNES subjects with a history of trauma and PTSD to PNES subjects with a history of trauma and no PTSD. This was repeated comparing PNES subjects with a history of trauma and no PTSD to PNES subjects without a history of trauma and no PTSD.

To explore whether subjective and objective memory measures were related, a correlation was run between the MCI scores and the four dependent variables.

Z scores were calculated for the CVLT Total Learning, LDFR, and Discriminability using population norms from the CVLT manual (Delis et al., 1987). Z scores for the RCFT Delay Trial scores were calculated using population norms provided in Spreen and Straus (1998). The RCFT Copy Trial z score was entered as a covariate for all analyses involving RCFT Delay Trial z scores. The mean z scores for the PNES and TLE groups were calculated for all four memory measures and t-tests were conducted to assess whether there was a difference between groups. The ratio of participants with z scores of -2.0 or below was calculated for the PNES and TLE groups. A Chi Square test was performed to assess whether there was a significant difference in the frequency of impairment between TLE and PNES groups as defined by the number of participants with a z score of -2.0 or lower. This was repeated for PNES patients with trauma as compared to PNES patients without trauma, PNES patients with sexual abuse as compared to PNES patients with all other trauma excluding sexual abuse, and for PNES patients with childhood abuse as compared to PNES patients with all other trauma excluding childhood abuse.

Post-hoc power analyses were conducted to assess whether there was enough power, given the sample sizes, to detect a clinically meaningful difference between groups. Criteria for determining meaningful clinical change were determined from published norms by evaluating the average number of points required to demonstrate a change of one standard deviation.

RESULTS

Preliminary Results

One PNES subject failed to meet the effort criteria; therefore, this participant along with their matched TLE control were eliminated from the study. All subsequent statistical analyses were conducted using the remaining 108 subjects. When PNES subjects who met the effort cutoff criteria were compared with PNES subjects who were missing effort measures, there was no statistically significant difference between the two groups for the CVLT Total Learning ($t = -.962$, $p = .340$), CVLT LDFR ($t = -.652$, $p = .517$), CVLT Discriminability ($t = -.200$, $p = .842$), or for RCFT Delay ($t = -1.153$, $p = .254$). Because the groups were comparable on effort, they were combined for all further analyses.

There was no significant difference between participants with and without depression on the CVLT Total Learning ($t = .501$, $p = .618$), CVLT LDFR ($t = .749$, $p = .457$), CVLT Discriminability ($t = .864$, $p = .390$), or for RCFT Delay Trial ($t = -.391$, $p = .751$). There were also no significant correlations between scores on the BAI, BDI/BDI-II, or MMPI-II depression scale and the CVLT Total Learning, CVLT LDFR, CVLT Discriminability, or the RCFT Delay Trial (see Table 7 for p values). Based on these results, it was concluded that depression and anxiety did not need to be controlled for in future analyses for this sample.

When PNES subjects were compared with TLE subjects using the Bonferroni procedure to control for type I error rate, there was no significant difference between the

groups on CVLT Total Learning (t = -1.378, p = .168), CVLT LDFR (t = -.548, p = .561), or for CVLT Discriminability (t = -.909, p = .365). A significant difference was found when comparing PNES subjects and TLE subjects on the RCFT Delay Trial (t = 2.713, p = .008), even after using the Bonferroni procedure (see Table 8). The correlation between the RCFT Copy Trial and RCFT Delay Trial was statistically significant (r = .549, p = .000), therefore the analysis was performed again with the Copy Trial score input as a covariate. When controlling for RCFT Copy Trial scores, the difference between PNES and TLE groups for the RCFT Delay Trial approached significance (F = 3.720, p = .056; see Table 8).

Post-hoc power analyses indicated sufficient power to detect the desired effect size. The desired effect sizes ranged from 0.67 to 1.12 for the four dependent variables with power to detect these effects ranging from 0.96 to 0.99.

Primary Results

There were no significant differences when PNES patients with a history of trauma were compared to both PNES patients without a history of trauma and TLE patients on CVLT Total Learning, CVLT LDFR, or CVLT Discriminability (see Table 8). The difference between PNES patients with a history of trauma, PNES patients without a history of trauma and TLE patients on RCFT Delay Trail scores only trended towards significance (F = 2.492, p = .088; see Table 9). Post-hoc power analyses indicated adequate power to detect the desired effect size. The desired effect sizes ranged from 0.29 to 0.48 for the four dependent memory measures with power to detect these effects ranging from 0.77 to 0.99.

When examining the impact of sexual abuse or childhood abuse on memory measures, results were similar. There were no significant differences when PNES patients with a history of sexual abuse were compared to both PNES patients without a history of trauma and PNES patients with a history of trauma other than sexual abuse on CVLT Total Learning, CVLT LDFR, CVLT Discriminability, or RCFT Delay Trial (see Table 10). There were also no significant differences when PNES patients with a history of childhood abuse were compared to PNES patients without a history of trauma and PNES patients with a history of trauma other than childhood abuse on CVLT Total Learning, CVLT Discriminability, or RCFT Delay Trial (see Table 11). There was a significant difference found between these groups for CVLT LDFR ($F = 3.426$, $p = .040$). A priori tests indicated that there was a significant difference between PNES patients with a history of childhood abuse and PNES patients with a history of trauma other than childhood abuse ($p = .041$), but there was not a significant difference between PNES patients without a history of trauma and PNES patients with a history of childhood abuse. For the analyses mentioned above involving sexual abuse and childhood abuse, post-hoc power analyses revealed that there was not sufficient power to detect the desired effect size for the CVLT Total Learning. The clinically relevant desired effect size was 0.30 and the power to detect this effect was 0.47. Power to detect the desired effect size of 0.40 for the CVLT LDFR was 0.73, which is slightly less than the desired power of 0.80 but is not drastically low. Finally, there was sufficient power to detect the desired effect sizes of 0.50 for the CVLT Discriminability and 0.51 for the RCFT Delay. Power to detect the desired effect size for CVLT Discriminability was 0.89 and power to detect the desired effect size for the RCFT Delay was 0.90.

Secondary Results

Trauma and PTSD are not independent groups. By definition, those with PTSD have had trauma but those who have experienced trauma do not necessarily have PTSD. As such, planned comparisons were conducted to investigate whether trauma may account for memory impairment independent from PTSD. Results indicated no significant difference between PNES subjects with a history of trauma with PTSD and PNES subjects with a history of trauma without PTSD (see Table 12). There was also no significant difference between PNES subjects with a history of trauma without PTSD and PNES subjects without a history of trauma (see Table 13).

Correlations between the MCI and CVLT Total Learning ($r = .094$, $p = .566$), CVLT LDFR ($r = .058$, $p = .722$), CVLT Discriminability ($r = -.023$, $p = .887$), and RCFT Delay Trial ($r = -.163$, $p = .314$) for PNES subjects were not statistically significant. Correlations between the MCI and CVLT Total Learning ($r = .192$, $p = .337$), CVLT LDFR ($r = .086$, $p = .671$), CVLT Discriminability ($r = -.059$, $p = .776$), and RCFT Delay Trial ($r = .038$, $p = .849$) for TLE subjects were also not statistically significant.

Mean z scores for the four dependent memory measures for PNES and TLE participants are listed in Table 14. The number of participants with z scores of -2.0 or less are listed in Table 15 for PNES and TLE groups. There were no significant differences between PNES and TLE participants on their mean z scores for CVLT Total Learning, LDFR, or Discriminability. There was a significant difference between z scores for RCFT Delay Trial when controlling for the Copy Trial z scores ($F = 4.226$, $p =$

.042). However, there were no significant differences between PNES and TLE participants on the number of z scores -2.0 or less for all four dependent memory measures. Mean z scores for the four dependent memory measures for PNES patients with a history of trauma and PNES patients without a history of trauma are listed in Table 16. There were no significant differences between PNES patients with and without a history of trauma on all four dependent memory measures. The number of participants with z scores of -2.0 or less are listed in Table 17 for PNES patients with and without a history of trauma. There were no significant differences between PNES patients with and without a history of trauma on the number of z scores -2.0 or less for all four dependent memory measures.

Mean z scores for the four dependent memory measures for PNES patients with a history of sexual abuse and PNES patients with a history of trauma excluding sexual abuse are listed in Table 18. There were no significant differences between PNES patients with a history of sexual abuse and PNES patients with a history of trauma other than sexual abuse on all four dependent memory measures. The number of participants with z scores of -2.0 or less are listed in Table 19 for PNES patients with a history of sexual abuse and PNES patients with a history of trauma other than sexual abuse. There were no significant differences between PNES patients with a history of sexual abuse and PNES patients with a history of trauma other than sexual abuse on the number of z scores -2.0 or less for all four dependent memory measures.

Mean z scores for the four dependent memory measures for PNES patients with a history of childhood abuse and PNES patients with a history of trauma excluding

childhood abuse are listed in Table 20. There were no significant differences between PNES patients with a history of childhood abuse and PNES patients with a history of trauma other than childhood abuse on CVLT Total Learning, CVLT LDFR, or RCFT Delay Trial. There was a significant difference in z scores between PNES patients with a history of childhood abuse and PNES patients with a history of trauma other than childhood abuse on the CVLT Discriminability ($t = 2.321$, $p = .030$). However, both PNES and TLE groups were in the normal range. The number of participants with z scores of -2.0 or less are listed in Table 21 for PNES patients with a history of childhood abuse and PNES patients with a history of trauma other than childhood abuse. There were no significant differences between PNES patients with a history of childhood abuse and PNES patients with a history of trauma other than childhood abuse on the number of z scores -2.0 or less for all four dependent memory measures.

DISCUSSION

To date, this is the first study to explore the relationship between psychological trauma and memory functioning in patients with PNES. Previous research has indicated that PNES patients have memory deficits similar to patients with ES, but few studies have investigated the reasons for PNES patient's memory deficits. Additionally, few studies assessing memory functioning in PNES patients have controlled for effort, depression, and anxiety, all factors which can confound findings. A number of previous studies have included patients with comorbid ES and PNES which can act as a potentially significant confound. Specifically, if PNES patients also have ES, their memory deficits may likely be a result of their ES. Finally, studies typically have not compared their findings to a normative sample. It has generally been the assumption that if PNES patient's memory functioning is equivalent to ES patient's memory functioning, then PNES patients were considered to have impaired memory. However, not all study samples are the same and it is possible that a study could have a high functioning ES group who in fact does not exhibit impaired memory functioning. As such, while studies have generally claimed that both ES and PNES groups exhibit memory "impairment," it is difficult to know the degree of impairment their study population is demonstrating.

The first aim of this study was to build upon previous studies that examined memory functioning in PNES patients as compared to ES patients by adding controls for effort, depression, and anxiety. This study also excluded patients with comorbid PNES and ES, eliminating the confound that this group poses. Based on previous literature, it was hypothesized that PNES and TLE groups would exhibit comparable verbal and non-

verbal memory performance even after controlling for effort, depression, and anxiety. This hypothesis was generally supported. There was not a statistically significant difference between PNES and ES groups on the three CVLT measures of memory, including Total Learning, LDFR, and Discriminability. While there was a statistically significant difference between PNES and ES patients on the RCFT Delay Trial, when the Copy Trial score was input as a covariate, that difference only tended toward significance.

These results support the findings by Binder et al. (1998) who reported no differences between PNES and ES groups on the Rey AVLT, RCFT, WMS-R Logical Memory, and CVMT. However, despite additional findings that PNES patients scored significantly lower on the PDRT and that PDRT scores were more strongly correlated with learning and memory scores in the PNES group than in the ES group, Binder et al., (1998) did not control for effort when evaluating memory performance (that is, they did not exclude those participants who failed effort tests). The results also support findings by Slater et al. (1995) and M.C. Brown et al. (1991) though neither of these groups controlled for effort. Furthermore, while all three studies assessed psychological functioning, only Binder et al. (1998) investigated whether there was a correlation between psychological functioning and memory performance. The other two studies did not control for depression or anxiety, both of which can impact memory performance. While the results of the current study and the study by Binder et al. (1998) indicated that depression and anxiety did not have an impact on memory functioning, every clinical sample is different, and since other studies did not control for depression and anxiety,

they may have contained an unknown confound. This is one of the few studies to control for effort, depression, and anxiety when examining memory performance in PNES and ES patients, and the results indicate that the memory functioning of PNES patients is similar to ES patients independent of effort, depression, and anxiety.

The results of this study are in sharp contrast with a study by Drane et al. (2006) which found that significantly more PNES patients as compared with ES patients did not put forth valid effort. When they compared PNES patients that did put forth valid effort to ES patients that put forth valid effort, PNES patients performed significantly better on neuropsychological measures. As a result, they claim that poor effort largely accounts for the impaired neuropsychological performance seen in PNES patients. However, the study by Drane et al. (2006) study was examining cognitive and global neuropsychological functioning rather than memory functioning specifically. They did not report patient performance for individual measures, so it is difficult to know how PNES patients compared with ES patients on memory measures specifically. They also did not exclude patients with IQ's below 70 or patients who had a history of major brain trauma, disease, or infection, all of which could act as possible confounds. In an effort to further explore this issue, Dodrill (2008) attempted to replicate the study by Drane et al. (2006) using "more broadly selected patients" from the same epilepsy center. Dodrill (2008) reported that Drane et al. (2006) eliminated 47% of the epilepsy sample for a variety of reasons and as a result, more severe ES patients were dropped from the study. Subsequently, Dodrill (2008) stated that Drane et al.'s (2006) sample was not representative of an ES population as a whole. Drane et al. (2006) also excluded patients

with recent seizures; Dodrill (2008) reported that this is unnecessary given that studies have indicated no cognitive effects of seizures even a few hours after they occurred. Finally, Drane et al. (2006) only included PNES patients who had been seen by full-time neuropsychologists. Dodrill (2008) reported that (as the result of a longstanding practice, established by Dodrill himself) PNES patients seen by full-time neuropsychologists at their center are typically more severe cases. Using a more inclusive selection criteria, Dodrill (2008) found that effort did not account for poor test performance in PNES patients any more than it did in ES patients. It appears that while it is important to control for effort, poor effort does not necessarily account for the memory deficits seen in PNES patients.

While several previous studies have found groupwise results similar to the present study, this is one of the first studies to compare participant's scores to population norms. Several studies have claimed that PNES patient's memory functioning was in the impaired range because their functioning was equivalent to that of a neurological group (ES patients). In this study, approximately 50% of scores from both groups were in the impaired range (as defined by a z score of -2.0 or less) on the CVLT Total Learning and LDFR. Less than 20% were in the impaired range on the CVLT Discriminability, which is not surprising since most people, including people with TLE, generally do well on recognition memory tasks. As a result, it appears that while a significant number of participants have impaired learning and recall, their recognition memory is relatively intact. Additionally, less than 15% of participant's scores were in the impaired range on the RCFT Delay Trial, indicating that nonverbal memory is relatively intact in most subjects. This is similar to the findings by Breier et al. (1998), one of the few studies to

report scores compared to population means. The authors reported that mean z scores on the Non-Verbal Selective Reminding Test were in the average range for both TLE and PNES patients. The findings in this study, along with the study by Breier et al. (1998) call into question the claims that PNES groups were in the impaired range for non-verbal memory measures simply because their raw scores were comparable to ES patient's scores. Therefore, in those studies where raw scores were not compared to norms, it is possible that even though both ES and PNES groups demonstrated similar performance, neither group's performance was in the impaired range. Despite these findings, it is important to note that depending upon which published norms are utilized there may be significant differences in whether a patient's score on the RCFT Delay is classified as being in the impaired range. The same score that would be classified as being in the average range utilizing the Spreen and Strauss (1998) norms may be classified as being in the borderline deficient range when utilizing more strict norms from Meyers and Meyers (1995). When comparing scores to population norms, it is important to consider that memory "impairment" will depend on the standard of the norms being utilized.

The second aim of this study was to explore whether psychological trauma is a contributing factor to the memory performance seen in PNES populations. It was proposed that cortisol, released as a result of traumatic stress, potentially leads to hippocampal damage and subsequent memory deficits. Therefore, it was hypothesized that PNES patients with a history of psychological trauma would exhibit significantly more impairment on verbal and non-verbal memory measures than PNES patients without a history of psychological trauma. In essence, it was hypothesized that those

PNES patients with a history of trauma would bring down the mean for the entire group, thereby accounting, in part, for the memory deficits previously seen in these patients. This hypothesis was not supported. The results indicated no differences on memory performance between PNES patients with and without a history of trauma. Additionally, there were no significant differences in normed z scores between the two groups. A little over half of the PNES patients with a history of trauma and approximately one third to one half of PNES patients without a history of trauma were in the impaired range on the CVLT Total Learning and CVLT LDFR. Fewer than 20% of patients from both groups were in the impaired range on the CVLT Discriminability or RCFT Delay.

This study also investigated whether a history of a specific type of trauma contributed differentially to the memory impairment in PNES populations. Because of the high rate of sexual abuse history in PNES populations and because abuse occurring in childhood may have a more profound impact on the developing brain, these two specific types of trauma were investigated. It was hypothesized that PNES patients with a history of sexual abuse and those with a history of childhood abuse would exhibit more memory impairment than PNES patients with histories of other types of trauma. These hypotheses were not supported. Memory performance in PNES patients with a history of childhood trauma or sexual abuse was comparable to memory performance for PNES patients with other types of trauma. There were also no significant differences on normed scores amongst the groups. Approximately 75% of PNES patients with a history of sexual abuse and a little over half of the patients with a history of trauma other than sexual abuse were in the impaired range on the CVLT Total Learning and CVLT LDFR. Less than

40% of patients in both groups were in the impaired range for the CVLT Discriminability and RCFT Delay Trial. Results were similar with regard to childhood abuse. This supports the notion that a significant percentage of PNES patients, regardless of whether they have a history of trauma, demonstrate impaired learning and recall memory, but that they are generally intact with regard to recognition memory and non-verbal memory.

To date, the only studies to investigate possible causes for the memory impairment seen in PNES populations have looked at effort, neuropathology, or psychopathology. While these studies have found that all three factors contributed to memory impairment, they were inconclusive as to whether these factors were more predictive of memory impairment in PNES groups than in ES groups (Binder et al., 1998; Binder et al., 1994; Cragar et al., 2006; Dodrill, 2008; Locke et al., 2006). Results from the current study suggest that inadequate effort and neuropathology do not account for impaired learning and recall memory in PNES patients since participants with poor effort or significant history of neurological insult were excluded from this study. MRI data for subjects was not available; however, neuropathology was approximated based upon reported history of neurological insult such as significant central nervous system trauma or disease. Additionally, while not all psychopathology was controlled for, this study did control for depression and anxiety. Historically, research has indicated that depression and anxiety negatively impact learning and memory (Bornstein, Baker, & Douglass, 1991; Sternberg & Jarvik, 1976); however, it appears that anxiety and depression do not account for the learning and recall memory impairment observed in PNES patients.

Results indicated that PTSD also did not account for the memory deficits in this PNES sample. While this may seem to contradict the numerous studies that have reported memory impairment in PTSD patients, in fact, approximately 50% of PNES patients with PTSD were in the impaired range for learning and recall memory. This is similar to the frequency of impairment seen in PNES patients as a whole and is also similar to the frequency of impairment in studies investigating PTSD and memory functioning. Therefore, PTSD does not account for the memory deficits in this PNES sample. It should be noted that it is difficult to draw conclusions from the results of this study given that there were only 12 participants who had a current, past, or rule out diagnosis of PTSD and only two participants who had current PTSD.

While it was not a primary aim of this study, the accuracy of subjective memory reporting was investigated to explore if ES or PNES patients are accurate at reporting the severity of their memory deficits. Few studies have examined the relationship between subjective ratings of memory and objectively measured memory functioning in this population. Fargo et al. (2004) reported that, with PNES patients, there was no correlation between objective memory scores, as measured by the WMS-III Word Lists, Verbal Paired Associates, and Logical Memory subtests and subjective memory functioning, as measured by the Memory subscale from the Quality of Life in Epilepsy Inventory-89 (QOLIE; Devinsky et al., 1995). They reported that ES patients accurately rated their memory functioning while PNES patients underestimated their memory functioning. The current study assessed whether there were correlations between subjective memory, as measured by the MCI and objective memory, as measured by the

four dependent memory variables. Results of this study partially contrasted the results of the study by Fargo et al. (2004) in that no correlations existed for either PNES or ES patients, suggesting that both PNES and ES patients are equally poor reporters of memory functioning.

Limitations

Though this is the first study to investigate the impact of psychological trauma on memory functioning in PNES patients, there are limitations to the conclusions from this study. One potential explanation for the lack of significant findings when comparing PNES patients with and without trauma is an inadequate sample size. While this study has one of the largest sample sizes when comparing PNES patients to TLE patients (only two other studies report larger sample sizes), when comparing PNES patients with and without trauma, the sample size is cut in half (N = 27). Despite this, post-hoc power analyses indicated that there was enough power to detect a clinically relevant effect size. When looking specifically at sexual abuse and childhood abuse, the sample sizes become even smaller. Post-hoc power analyses indicated that the study lacked sufficient power to detect a clinically relevant effect size for analyses examining learning (CVLT Total Learning) and power was slightly less than desirable for analyses examining recall memory (CVLT LDFR). It is possible that replicating the study with a larger sample of PNES patients with and without trauma (as well as with and without sexual abuse and childhood abuse) would result in significant findings.

While this study is one of the few to compare findings to population norms, it did not utilize a normal control group. Comparison of PNES patients to a simultaneously

collected normal control group might allow for a deeper understanding of the severity of the memory impairment in PNES subjects. A control sample would be located within the same geographic region and as a result, control subjects would potentially be better demographic matches to the study sample. To date, only one study investigating differences between PNES and ES patients on neuropsychological functioning has utilized a normal control group. While Binder et al. (1998) compared PNES and ES patients to normal controls, their normal control group was limited in that it was an existing data set that did not include many of the neuropsychological measures (including memory measures) given to the ES and PNES groups. Despite the challenges that it entails, utilizing a normal control group in addition to a TLE group could further enhance this study.

The impact of AED medication or other medications on memory functioning was not controlled for in this study. Locke et al. (2006) reported that more AEDs were associated with decreased memory functioning in both ES and PNES patients. They reported an average of a 2.5 point decline on composite memory scores for each AED. The authors also examined the differential effects of older generation AEDs versus newer generation AEDs because older AEDs are generally understood to have more cognitive side effects than newer AEDs. However, they reported no differences between older versus newer AEDs on cognitive functioning, including memory. They also examined the impact of other medications, such as medications for depression, hypertension, thyroid dysfunction, and cardiac abnormalities on memory functioning. Interestingly, they found a positive correlation between the number of medications and memory

functioning. They reported an increase of 1.5 points on composite memory scores for each additional medication. They hypothesized that this increase may be the result of more effectively controlled health issues with medication. Based on these results it is clear that both AEDs and other medication can potentially impact memory functioning either positively or negatively. However, it should be noted that the clinical implications of composite memory score changes in either direction are unclear. Because the current study did not analyze data on the number of AED or other medications used by participants, it cannot be determined that medication usage was equivalent between ES and PNES groups. Therefore, it is possible that medication usage may have differentially impacted memory functioning between the two groups in this study. In essence, while the two groups demonstrated equivalent memory functioning, it is possible that if one group was taking significantly more medications with cognitive side effects, their scores could have been significantly higher if they had not been taking the medications. However, controlling for the cognitive impact that medications pose is challenging due to the multiplicity of factors that could potentially impact memory functioning, such as: number and type of medications, dosage, and medication interactions.

Because this was a retrospective rather than a prospective study, it was difficult to ensure that all psychological and neuropsychological measures were available for each participant. As reported, only a portion of the sample was administered the depression and anxiety measures, and as a result, analyses were conducted using only a subset of the sample (~60-70%). Ideally, a prospective study would ensure that no measures were missing, so that all analyses could be conducted for the entire sample. Additionally, only

a portion of the PNES sample was administered effort measures. Since there were no significant differences in memory performance between those participants with and without effort measures, all subjects were included in subsequent analyses. However, it would have been ideal to have data on effort measures for the entire sample. Despite this, it should be noted that the advantage of conducting a retrospective study is that it allows for the utilization of patient data for a more extended period of time than would typically be possible with a prospective study, thereby permitting a larger sample size. For example, in the current study, to obtain a clean sample of 54 PNES patients who did not have comorbid ES or a significant history of neurological insult, and who also demonstrated adequate effort on testing, required review of seven years worth of records. Many prospective studies do not typically cover time periods of this length.

Another disadvantage of conducting a retrospective study is that trauma history for the TLE group was not known as this information is not systematically obtained in all patients at the NYU CEC. Patients with a diagnosis of PNES or those who are suspected of having PNES are typically given psychiatric evaluations since PNES is a psychiatric condition. TLE patients on the other hand are typically not given psychiatric evaluations unless there is a suspicion of or previous diagnosis of psychiatric illness in addition to TLE. If patients are not given a psychiatric evaluation then trauma history is typically unknown. It is possible that the unknown trauma history in the TLE group acted as a potential confound to this study.

Finally, because this was a retrospective study, data regarding ethnicity and socioeconomic status (SES) were not available for all participants. As a result, it was not

possible to examine whether there were correlations between memory performance and these demographic variables. It is possible that one or both of these two variables could help explain why approximately 50% of PNES patients demonstrated memory impairment while the other 50% performed within normal limits.

Directions for Future Research

Based upon the results of this study and previous studies, it is recommended that future studies look to replicate the finding of comparable memory performance between PNES and ES populations while controlling for poor effort and mood. In fact, all studies exploring any type of neuropsychological functioning in ES and PNES populations would benefit from controlling for effort since failure to meet effort criteria has been reported in as much as 30-50% of these populations (Dodrill, 2008; Drane et al., 2006).

It is also recommended that future studies investigating memory utilize a TLE control group rather than a control group composed of patients with generalized epilepsy or mixed seizure types. This will help to ensure that neurological damage is more confined to the temporal lobes and as such, the resulting neuropsychological deficits may be more specific to memory deficits rather than more global and variable neurological deficits that may skew findings.

If future studies continue to examine the contribution of a history of psychological trauma to memory deficits in PNES patients, then they would benefit from controlling for trauma history in the control group to prevent a possible confound. They would also benefit from a larger sample size that should be determined by conducting a-priori power

analyses. Future studies would benefit from collecting data on SES and ethnicity to investigate any potential correlations between these factors and memory functioning.

Based upon the report by Locke et al. (2006) indicating a negative impact of AEDs on memory functioning and a positive impact of other medications on memory functioning, studies would benefit from further examining the role of these medications and subsequently controlling for their effect on memory functioning. While Locke et al. (2006) did not report differences between PNES and ES groups on the number of AED or other medications used; it is difficult to predict whether this would be true for all study samples. As such, controlling for medications with known cognitive side effects would limit unnecessary confounds and help to further delineate the reasons for memory impairment in PNES patients.

Future studies should continue to report results in comparison to either population means or a normal control group. This will help to delineate the degree of "impairment" these populations demonstrate on all neuropsychological functioning rather than automatically assuming impairment based upon comparable raw scores and the general knowledge that ES populations typically demonstrate impairment. It also allows for transparency when making claims of impairment as readers can see exactly how the researchers defined clinical impairment.

Finally, the factors that account for the memory deficits seen in PNES patients continue to remain largely unknown. Consequently, future studies should continue to identify and investigate possible causes of the memory impairment in PNES patients. While there are other risk factors for developing PNES such as a family history of

epilepsy, a family history of psychiatric illness, and living in rural settings, these are not necessarily risk factors for memory impairment. As such, it remains elusive as to why memory deficits often go hand in hand with a diagnosis of PNES. It may be enlightening to investigate whether there are differences in memory functioning between PNES patients diagnosed with conversion disorder and conversion disorder patients with different neurological presentations such as numbness or paralysis. If memory impairment is confined to PNES patients only, then future studies could subsequently examine what is novel about PNES.

Similar to studies examining memory deficits in PTSD, future research could explore whether memory impairment is a risk factor for the development of PNES or whether PNES is a risk factor for the development of memory deficits. This is difficult to investigate because premorbid functioning in PNES patients is rarely known. However, inferring previous functioning through school records, occupational attainment, and exams (e.g., SAT exam) would potentially provide insight into the direction of this relationship. Either way, PNES patients demonstrate memory impairment and what led to this impairment continues to remain unclear.

Conclusions

Multiple studies have replicated the finding that PNES patients demonstrate memory impairment, but the reasons for their memory impairment remain poorly understood. To date, the majority of studies examining memory and neuropsychological functioning in PNES patients have done so in an attempt to identify ways of differentiating PNES from ES patients. Studies have typically explored whether there

were differences between PNES and ES patients in various domains of functioning (e.g., memory, effort, and psychopathology) in the hopes of potentially using these measures to aid in the diagnostic process. The current study is one of the few studies thus far to examine a potential reason why the memory deficits exist. Similar to studies in PTSD populations, in this study, only a portion (approximately 50%) of PNES patients were in the impaired range when compared to population norms. As a result, the question arises as to what is different about those patients who demonstrate impairment from those who do not. While replication of all studies is important, the results of this study suggest that trauma is not what accounts for the memory impairment in PNES patients. It may be the case that trauma is only associated with memory impairment when it is accompanied by the development of PTSD.

Continued investigation into why some PNES patients have memory impairment is important because it augments our understanding of the disorder as a whole. Furthermore, it provides greater insight into the interaction between psychological and neuropsychological functioning. PNES can be a debilitating condition for many people and can have a disruptive impact on daily life. PNES patients typically report poor quality of life as reflected by mental, physical, and social well-being (Breier et al., 1998). Additionally, the memory impairment that can accompany PNES may further exacerbate the challenges these patients face. A more thorough understanding of why PNES patients have memory deficits would potentially lead to better treatment of the disorder. This in turn, could lead to an improved quality of life, reducing some of the psychological distress associated with the disorder. Reduction of psychological distress may then help

to alleviate other PNES symptoms, creating a positive spiral effect that further improves patients' quality of life.

It is hoped that this study will stimulate thought and exploration of the variables related to the memory impairment seen in PNES patients and that future research will continue to delineate the variables, thereby allowing for better understanding of the disorder and improved treatment.

Table 1 Descriptive Characteristics of Study Population.

Variable	PNES N = 55	TLE N = 55	p-Value[1]
Gender: Number (%) Female	45 (81.8%)	45 (81.8%)	1.00[2]
Age (in years)	37.42 (10.5)	37.96 (11.3)	.79
Years of Education	14.95 (2.4)	14.44 (2.3)	.26
WAIS-R/III VIQ	102.7 (14.9)[3]	99.8 (14.9)	.31
WAIS-R/III PIQ	100.7 (16.6)[3]	96.4 (14.1)	.15

Note. All data are expressed as mean (SD), except Gender, which is number of female participants (%). WAIS-R/III = Weschler Adult Intelligence Scale (revised and 3rd edition). VIQ = Verbal Intelligence Quotient. PIQ = Performance Intelligence Quotient. [1]Independent samples t-test. [2]Chi Square. [3]n = 54, one missing score; however, participant met minimum IQ requirement based upon Weschler Abreviated Scale of Intelligence (WASI) score (Wechsler, 1999).

Table 2 Descriptive Characteristics of PNES Population.

Variable	PNES w/ Trauma[1] N = 28	PNES w/o Trauma[2] N = 27	p-Value[3]
Gender: Number (%) Female	25 (89.3%)	20 (74.1%)	.144[4]
Age (in years)	36.57 (9.62)	38.30 (11.47)	.548
Years of Education	14.75 (2.58)	15.15 (2.25)	.545
WAIS-R/III VIQ	99.39 (15.58)	106.35 (13.56)[5]	.087
WAIS-R/III PIQ	97.75 (16.56)	103.77 (16.28)[5]	.184

Note. All data are expressed as mean (SD) except Gender, which is number of female participants (%). WAIS-R/III = Weschler Adult Intelligence Scale (revised and 3rd edition). VIQ = Verbal Intelligence Quotient. PIQ = Performance Intelligence Quotient). [1]PNES w/ Trauma = PNES patients with a history of trauma. [2]PNES w/o Trauma = PNES patients without a history of trauma. [3] Independent samples t-test. [4]Chi Square. [5]n = 26, one missing score; however, participant met minimum IQ requirement based upon Weschler Abreviated Scale of Intelligence (WASI) score (Wechsler, 1999).

Table 3 Physical and Sexual Abuse Coding.

Sexual Abuse Invasiveness	Physical Abuse Severity
• 0 = None • 1 = Other sexual abuse not involving genital contact such as fondling • 2 = Manual genital contact • 3 = Oral, anal, or genital penetration	• 0 = None • 1 = Shoved, slapped • 2 = Struck by a fist • 3 = Struck or deliberately injured by an object • 4 = Injury requiring acute medical attention

Table 4 Trauma Prevalence Frequencies for PNES Subjects.

TRAUMA TYPE	**YES** N (%)	**NO** N (%)
Lifetime Trauma	28 (50.9%)	27 (49.1%)
Childhood Abuse	16 (29.1%)	39 (70.9%)
Childhood Sexual Abuse	9 (16.4%)	46 (83.6%)
Childhood Physcial Abuse	9 (16.4%)	46 (83.6%)
Adult Abuse	14 (25.5%)	41 (74.5%)
Adult Sexual Abuse	8 (14.5%)	47 (85.5%)
Adult Physical Abuse	8 (14.5%)	47 (85.5%)
Other Trauma	8 (14.5%)	47 (85.5%)

Note. All data are expressed as number of participants (%).

Table 5 Frequency for Level of Abuse Severity for PNES Subjects.

	Abuse Dimension Severity Code[1]			
	1 N (%)	**2 N (%)**	**3 N (%)**	**4 N (%)**
Childhood Sexual Abuse[2]	1 (1.8%)	3 (5.5%)	3 (5.5%)	NA
Childhood Physical Abuse	0	5 (9.1%)	4 (7.3%)	0
Adult Sexual Abuse	1 (1.8%)	0	7 (12.7%)	NA
Adult Physical Abuse	1 (1.8%)	0	6 (10.9%)	1 (1.8%)

Note. All data are expressed as number of participants (%). [1]Refer to Table 3 for explanation of abuse dimension severity codes; in all cases, greater scores correspond to greater severity of the abuse dimension. [2]Two participants were missing childhood sexual abuse severity.

Table 6 Frequency of PTSD for PNES Subjects.

	YES N (%)	**NO** N (%)
Any PTSD	12 (21.8%)	43 (78.2%)
Past PTSD	3 (3.6%)	52 (94.5%)
Current PTSD	2 (3.6%)	53 (96.4%)
Rule-out PTSD	7 (12.7%)	48 (87.3%)

Note. All data are expressed as number of participants (%).

Table 7 Correlations between Depression/Anxiety Raw Scores and Dependent Memory Measures.

		BAI	BDI/ BDI-II	MMPI-II Depression
CVLT Total Learning	Pearson Correlation	.131	.105	.162
	Sig. (2-tailed)	.311	.431	.164
	N	62	63	75
CVLT LDFR	Pearson Correlation	-.003	.051	.130
	Sig. (2-tailed)	.983	.691	.265
	N	62	63	75
CVLT Discriminability	Pearson Correlation	-.102	-.081	.057
	Sig. (2-tailed)	.436	.533	.630
	N	61	62	73
RCFT Delay	Pearson Correlation	-.040	.014	.019
	Sig. (2-tailed)	.757	.913	.817
	N	62	63	75

No correlations were statistically significant.

Table 8 Comparisons of PNES and TLE Patients on Neuropsychological Measures of Memory.

	PNES N = 54	**TLE** N = 54	**F Value**	**P Value**
CVLT Total Learning	49.26 (10.34)	52.02 (10.34)	-1.378	.168
CVLT LDFR	9.98 (3.31)	10.37 (3.61)	-.548	.561
CVLT Discriminability	92.00 (7.26)[1]	93.25 (6.86)	-.909	.365
RCFT Delay w/ Copy as covariate	15.65 (5.65)	12.50 (6.39)	3.720	.056

Note. All data are expressed as mean (SD). *Significant at $p < .05$ level. [1]N = 52 (missing Discriminability scores for two participants).

Table 9 Comparisons of PNES Patients with a History of Trauma, PNES Patients without a History of Trauma, and TLE Patients on Neuropsychological Measures of Memory.

	PNES w/o Trauma[1] N = 27	PNES w/ Trauma[2] N = 27	TLE N = 54	F Value	P Value
CVLT Total Learning	50.85 (11.08)	47.67 (9.47)	52.02 (10.34)	1.607	.205
CVLT LDFR	10.22 (3.69)	9.74 (2.92)	10.37 (3.61)	.229	.742
CVLT Discriminability	91.37 (8.18)	92.68 (6.22)[3]	93.25 (6.86)	.633	.533
RCFT Delay w/ Copy as covariate	14.83 (6.18)	16.46 (5.04)	12.50 (6.39)	2.492	.088

Note. All data are expressed as mean (SD). *Significant at $p < .05$ level. [1]PNES w/o Trauma = PNES patients without a history of trauma. [2]PNES w/ Trauma = PNES patients with a history of trauma. [3]N = 25 (missing Discriminability scores for two participants).

Table 10 Comparison of PNES Patients with a History of Sexual Abuse to PNES Patients with a History of Trauma Other than Sexual Abuse and PNES Patients without a History of Trauma on Neuropsychological Measures of Memory.

	PNES w/o Trauma[1] N = 27	**PNES w/ Sexual Abuse[2]** N = 15	**PNES w/ Other Trauma[3]** N = 12	**F Value**	**P Value**
CVLT Total Learning	50.85 (11.08)	47.53 (10.38)	47.83 (8.65)	.635	.534
CVLT LDFR	10.22 (3.69)	10.00 (3.42)	9.42 (2.23)	.240	.788
CVLT Discriminability	91.37 (8.18)	92.40 (7.06)	93.10 (5.02)[4]	.232	.794
RCFT Delay w/ Copy as covariate	14.83 (6.18)	17.37 (5.01)	15.33 (5.05)	.762	.472

Note. All data are expressed as mean (SD). [1]PNES w/o Trauma = PNES patients without a history of trauma. [2]PNES w/ Sexual Abuse = PNES patients with a history of sexual abuse. [3]PNES w/ Other Trauma = PNES patients with a history of trauma other than sexual abuse. [4]N = 10 (missing Discriminability scores for two participants).

Table 11 Comparison of PNES Patients with a History of Childhood Abuse to PNES Patients with a History of Trauma Other than Childhood Abuse and PNES Patients without a History of Trauma on Neuropsychological Measures of Memory.

	PNES w/o Trauma[1] N = 27	PNES w/ Childhood Abuse[2] N = 15	PNES w/ Other Trauma[3] N = 12	F Value	P Value
CVLT Total Learning	50.85 (11.08)	50.13 (9.26)	44.58 (9.18)	1.641	.204
CVLT LDFR	10.22 (3.69)	11.13 (2.59)	8.00 (2.37)	3.426	.040*
CVLT Discriminability	91.37 (8.18)	95.36 (3.82)[4]	89.27 (7.14)[5]	2.516	.091
RCFT Delay w/ Copy as a covariate	14.83 (6.18)	16.77 (5.54)	16.08 (4.54)	.814	.499

Note. All data are expressed as mean (SD). *Significant at $p < .05$ level. [1]PNES w/o Trauma = PNES patients without a history of trauma. [2]PNES w/ Childhood Abuse = PNES patients with a history of childhood abuse. [3]PNES w/ Other Trauma = PNES patients with a history of trauma other than childhood abuse. [4]N = 14 (missing Discriminability score for one participant). [5]N = 11 (missing Discriminability score for one participant).

Table 12 Comparison of PNES Patients with a History of Trauma without PTSD to PNES Patients with a History of Trauma and PTSD on Neuropsychological Measures of Memory.

	PNES w/ Trauma & w/o PTSD[1] N = 15	PNES w/ Trauma & PTSD[2] N = 12	t Value	P Value
CVLT Total Learning	48.20 (6.90)	47.00 (12.27)	.303	.766
CVLT LDFR	9.60 (2.80)	9.92 (3.20)	-.275	.785
CVLT Discriminability	92.64 (4.86)[3]	95.36 (3.82)[4]	-.033	.974
RCFT Delay	15.33 (4.92)	17.88 (5.02)	-1.322	.198

Note. All data are expressed as mean (SD). [1]PNES w/ Trauma & w/o PTSD = PNES patients with a history of trauma without PTSD. [2]PNES w/ Trauma & PTSD = PNES patients with a history of trauma and PTSD. [3]N = 14 (missing Discriminability score for one participant). [4]N = 11 (missing Discriminability score for one participant).

Table 13 Comparison of PNES Patients without a History of Trauma to PNES Patients with a History of Trauma and without PTSD on Neuropsychological Measures of Memory.

	PNES w/o Trauma[1] N = 27	**PNES w/ Trauma & w/o PTSD[2]** N = 15	**t Value**	**P Value**
CVLT Total Learning	50.85 (11.08)	48.20 (6.90)	.838	.407
CVLT LDFR	10.22 (3.69)	9.60 (2.80)	.567	.574
CVLT Discriminability	91.37 (8.18)	92.64 (4.86)	-.534	.597
RCFT Delay	14.83 (6.18)	15.33 (4.92)[3]	-.269	.789

Note. All data are expressed as mean (SD). [1]PNES w/o Trauma = PNES patients without a history of trauma. [2]PNES w/ Trauma & w/o PTSD = PNES patients with a history of trauma and without PTSD. [3]N = 14 (missing Discriminability score for one participant).

Table 14 Comparison of Z score Means for TLE and PNES Patients on Neuropsychological Measures of Memory.

	TLE Mean (SD) N = 54	**PNES** Mean (SD) N = 54	**t(F) Value**	**p Value**
CVLT Total Learning	-1.17 (1.32)	-1.61 (1.33)	-1.718	.089
CVLT LDFR	-1.54 (1.79)	-2.0 (1.85)	-1.321	.189
CVLT Discriminability	-.52 (.99)	-.69 (1.02)[1]	-.892	.374
RCFT Delay w/ Copy as a covariate	-.81 (.92)	-.33 (.84)	F = 4.226	.042*

[1]N = 52 (missing Discriminability scores for two participants). *Significant at p <.05 level.

Table 15 Comparison of TLE and PNES Groups on the Number of Participants with z scores Less than or Equal to -2.0 on Neuropsychological Measures of Memory.

	TLE Number of Patients with a z score ≤ -2.0 (%)	**PNES** Number of Patients with a z score ≤ -2.0 (%)	**Chi Square p value**
CVLT Total Learning	15 (27.8%)	24 (44.4%)	.071
CVLT LDFR	26 (48.1%)	32 (59.3%)	.247
CVLT Discriminability	7 (13.0%)	9 (17.3%)[1]	.532
RCFT Delay	6 (11.1%)	2 (3.7%)	.142

[1]N = 52 (missing Discriminability scores for two participants).

Table 16 Comparison of Z score Means for PNES Patients with a History of Trauma and PNES Patients without a History of Trauma on Neuropsychological Measures of Memory.

	PNES w/ Trauma[1] Mean (SD) N = 27	**PNES w/o Trauma[2]** Mean (SD) N = 27	**t(F) Value**	**p Value**
CVLT Total Learning	-1.91 (1.32)	-1.31 (1.30)	1.673	.100
CVLT LDFR	-2.37 (1.84)	-1.63 (1.82)	1.485	.143
CVLT Discriminability	-.56 (.92)[3]	-.82 (1.11)	-.898	.373
RCFT Delay w/ Copy as a covariate	-.22 (.83)	-.43 (.98)	F = -.916	.343

[1]NES w/ Trauma = PNES patients with a history of trauma. [2]PNES w/o Trauma = PNES patients without a history of trauma. [3]N = 25 (missing Discriminability scores for two participants).

Table 17 Comparison of PNES Patients with a History of Trauma and PNES Patients without a History of Trauma on the Number of Participants with z Scores Less than or Equal to -2.0 on Neuropsychological Measures of Memory.

	PNES w/ Trauma[1] Number of Patients with a z score ≤ -2.0 (%)	**PNES w/o Trauma[2]** Number of Patients with a z score ≤ -2.0 (%)	**Chi Square p value**
CVLT Total Learning	15 (55.6%)	9 (33.3%)	.100
CVLT LDFR	17 (63.0%)	15 (55.6%)	.580
CVLT Discriminability	4 (16.0%)[3]	5 (18.5%)	.810
RCFT Delay	0 (0.0%)	2 (7.4%)	.150

[1]PNES w/ Trauma = PNES patients with a history of trauma. [2]PNES w/o Trauma = PNES patients without a history of trauma. [3]N = 25 (missing Discriminability score for two participants).

Table 18 Comparison of Z score Means for PNES Patients with a History of Sexual Abuse and PNES Patients with a History of Trauma Other than Sexual Abuse on Neuropsychological Measures of Memory.

	PNES w/ Sexual Abuse[1] Mean (SD) N = 15	**PNES w/ Other Trauma[2]** Mean (SD) N = 12	**t(F) Value**	**p Value**
CVLT Total Learning	-2.05 (1.41)	-1.73 (1.24)	-.605	.551
CVLT LDFR	-2.47 (2.10)	-2.25 (1.55)	-.298	.768
CVLT Discriminability	-0.6 (1.06)	-.50 (.71)[3]	-.262	.796
RCFT Delay w/ Copy as a covariate	-.284 (.73)	-.28 (.73)	F = .451	.640

[1]PNES w/ Sexual Abuse = PNES patients with a history of sexual abuse. [2]PNES w/ Other Trauma = PNES patients with a history of trauma other than sexual abuse. [3]N = 10 (missing Discriminability scores for two participants).

Table 19 Comparison of PNES Patients with a History of Sexual Abuse and PNES Patients with a History of Trauma Other than Sexual Abuse on the Number of participants with Z Scores Less Than or Equal to -2.0 on Neuropsychological Measures of Memory.

	PNES w/ Sexual Abuse[1] Number of Patients with a z score ≤ -2.0 (%)	**PNES w/ Other Trauma[2]** Number of Patients with a z score ≤ -2.0 (%)	**Chi Square**
CVLT Total Learning	6 (40.0%)	6 (50.0%)	.227
CVLT LDFR	10 (66.7%)	7 (58.3%)	.779
CVLT Discriminability	3 (20.0%)	1 (10.0%)[3]	.788
RCFT Delay	0	0	NA

[1]PNES w/ Sexual Abuse = PNES patients with a history of sexual abuse. [2]PNES w/ Other Trauma = PNES patients with a history of trauma other than for sexual abuse. [3]N = 10 (missing Discriminability scores for two participants).

Table 20 Comparison of Z score Means for PNES Patients with a History of Childhood Abuse and PNES Patients with a History of Trauma Other than Childhood Abuse on Neuropsychological Measures of Memory.

	PNES w/ Childhood Abuse[1] Mean (SD) N = 15	**PNES w/ Other Trauma[2]** Mean (SD) N = 12	**t(F) Value**	**p Value**
CVLT Total Learning	-1.73 (1.37)	-2.13 (1.28)	.789	.438
CVLT LDFR	-1.80 (1.90)	-3.08 (1.62)	1.884	.071
CVLT Discriminability	-.21 (.70)[3]	-1.00 (1.00)[4]	2.312	.030*
RCFT Delay w/ Copy as a covariate	-.21 (.70)	-.23 (.70)	F = .461	.633

[1]PNES w/ Childhood Abuse = PNES patients with a history of childhood abuse. [2]PNES w/ Other Trauma = PNES patients with a history of trauma other than childhood abuse. [3]N = 14 (missing Discriminability score for one participant). [4]N = 11 (missing Discriminability score for one participant). *Significant at $p < .05$ level.

Table 21 Comparison of PNES Patients with a History of Childhood Abuse and PNES Patients with a History of Trauma Other than Childhood Abuse on the Number of Participants with Z Scores Less Than or Equal to -2.0 on Neuropsychological Measures of Memory.

	PNES w/ Childhood Abuse[1] Number of Patients with a z score ≤ -2.0 (%)	**PNES w/ Other Trauma[2]** Number of Patients with a z score ≤ -2.0 (%)	**Chi Square p value**
CVLT Total Learning	7 (46.7%)	8 (25.0%)	.151
CVLT LDFR	8 (53.3%)	9 (75.0%)	.449
CVLT Discriminability	1 (7.1%)[3]	3 (27.3%)[4]	.406
RCFT Delay	0	0	NA

[1]PNES w/ Childhood Abuse = PNES patients with a history of childhood abuse. [2]PNES w/ Other Trauma = PNES patients with a history of trauma other than childhood abuse. [3]N = 14 (missing Discriminability score for one participant). [4]N = 11 (missing Discriminability score for one participant). *Significant at $p < .05$ level.

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