Epilepsy & Behavior 37 (2014) 82–86

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Cognitive differences between patients who have psychogenic nonepileptic seizures (PNESs) and posttraumatic stress disorder (PTSD) and patients who have PNESs without PTSD

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ARTICLE INFO

Article history:
Received 11 February 2014
Revised 16 May 2014
Accepted 5 June 2014
Available online 7 July 2014

Keywords:
Psychogenic nonepileptic seizures
Posttraumatic stress disorder
Cognitive function
Memory

ABSTRACT

Objectives: The objective of this study was to examine cognitive and clinical differences among three groups of patients diagnosed with psychogenic nonepileptic seizures (PNESs): those with posttraumatic stress disorder (PTSD), those with a history of trauma but no PTSD, and those without a history of trauma.

Methods: Seventeen patients who were confirmed to have PTSD based on the Trauma Symptom Inventory-2 (TSI-2) and clinical interview were compared with 29 patients without PTSD who had experienced trauma and 17 patients who denied experiencing trauma. We analyzed demographic data, psychiatric information, trauma characteristics, and neuropsychological variables in these groups.

Results: Our study revealed that patients with PNESs with comorbid PTSD performed significantly worse on episodic verbal memory (narrative memory); had greater self-reported Total, Verbal, and Visual Memory impairments; and had higher substance abuse history and use of psychopharmacological agents compared with patients without PTSD regardless of a history of trauma.

Conclusion: The present study showed that patients with PNESs diagnosed with PTSD exhibited memory functions that were significantly different from those in patients with PNESs who do not carry a diagnosis of PTSD (regardless of history of trauma). Furthermore, these specific cognitive findings in narrative memory are consistent with those reported in patients with PTSD alone. The present findings contribute to further identifying discrete intragroup differences within PNESs. Identifying a specific psychopathological subgroup such as PTSD will allow clinicians to accurately select treatment.

1. Introduction

Psychogenic nonepileptic seizures (PNESs) are events that resemble epileptic seizures but lack electrophysiological correlates or clinical evidence for epilepsy, and, instead, there is evidence for a psychogenic nature. Up to 90% of patients with PNESs have been reported to have histories of significant traumatic experiences, with particularly high instances of childhood sexual and physical abuse, compared with control groups and the general population [1,2]. Previous studies have obtained percentages of patients with PNES and PTSD features ranging from 22 to 100% [3,4]. In a recent study, our program reported that 45 (73.8%) out of 61 patients experienced at least one traumatic event in their lifetime, and 12 (26.66%) of those 45 fulfilled the criteria for posttraumatic stress disorder (PTSD) based on the Trauma Symptom Inventory-2 (TSI-2) [5]. This high variability in percentages of patients with PNESs with comorbid PTSD could be due to the inconsistency in measures used to diagnose PTSD across these studies or differences between samples with PNESs.

The long-term effects that trauma and subsequent PTSD may have on cognitive development have been the focus of trauma research for decades [6,7]. Investigations of PTSD not associated with PNESs have found discrete psychological and neuropsychological findings that differentiate this group of patients from healthy controls as well as from individuals with a history of trauma who have not developed PTSD. The most robust cognitive deficits appear to involve memory systems, with patients experiencing greater impairments in verbal declarative memory function along with relatively intact visual memory [8–27]. In recent years, the importance of including performance validity testing into neuropsychological batteries to avoid erroneous conclusions regarding cognitive impairments has been recommended [28]. Indeed, with regard to PTSD, a study this year [29] found that failure

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http://dx.doi.org/10.1016/j.yebeh.2014.06.009
1525-5050/

on a performance validity test (Word Memory Test) was associated with poorer performance on almost all cognitive tests and concluded that the assessment of respondent validity is necessary when evaluating this population.

Patients with PNESs have also been reported to perform below normal limits on neuropsychological testing compared with standardized norms [1,30] on a range of cognitive functions with no particular deficit pattern. Some authors [31] have revealed that a substantial number of patients with PNESs are not putting forth sufficient effort on cognitive testing, which might explain many of these reported cognitive weaknesses. Other researchers [32] suggest that these numbers are being overestimated depending on the design of the study. In view of this debate, performance validity testing is a necessary part of standard neuropsychological batteries with patients with PNESs and PTSD. The goal of our present study was to determine whether patients dually diagnosed with PNESs and PTSD have a cognitive pattern which is similar to the patterns reported in the literature for PTSD. If this were true, these particular patients may benefit more from empirically validated PTSD treatment as a first line of action rather than other less specific treatments.

2. Material and methods

This study included 79 consecutive patients with a diagnosis of PNESs confirmed with inpatient video-EEG monitoring who went on to complete a comprehensive neuropsychological battery between 2008 and 2013 and who had an IQ > 70.

All of the subjects were interviewed by a neuropsychologist who assessed for a history of trauma. Trauma was classified as physical abuse (i.e., bruising, broken bones, whip marks, stab wounds, concussions resulting from blows to the head), rape/sexual abuse (i.e., touching/fondling and/or forced oral sex or vaginal/anal intercourse), loss or death of significant other (i.e., death of a child, unwanted estrangement, and prolonged shunning from family), severe medical history (multiple and painful surgical interventions or treatments), witnessing the abuse of another (i.e., seeing a sibling or mother being raped or beaten), and severe emotional abuse (repeated verbal insults, marginalization and neglect by caretakers, or continuous verbal bullying). A tally of types of trauma was recorded. Since some patients had experienced multiple traumatic events, age of the first traumatic episode was classified as “age of initial trauma.” A diagnosis of PTSD was made based on the information obtained from the clinical interview (according to DSM-IV criteria) combined with the scores from the TSI-II. Charts were reviewed to determine whether there was a history of traumatic head injury with or without loss of consciousness. Current medications being taken at the time of the assessment were recorded; patients reported whether these were being prescribed to treat depression, anxiety, psychotic symptoms, and/or sleep disorders. Age at PNES onset and duration as well as other demographic variables were also logged.

Patients were categorized into one of three groups: Group 1 reported psychological trauma and were diagnosed with PTSD, Group 2 reported a history of psychological trauma but failed to fulfill criteria for PTSD, and Group 3 denied a history of trauma.

2.1. Exclusion criteria

The initial number of 79 patients was reduced to 63 because of the following exclusions: 2 were found to have a dual diagnosis of epilepsy and PNESs, and 14 were classified by the neuropsychologist as putting forth insufficient effort (malingering) based on published cutoffs on the Test of Memory Malingering (TOMM) [33], a test of performance validity, behavioral observations suggestive of deficient effort, and/or verification of an active pursuit of a personal injury suit or a disability petition.

2.2. Measures

The standard battery of tests administered to our patients with PNESs at the Northeast Regional Epilepsy Group includes six cognitive tests. These measure intelligence, verbal and visual memory, executive functions, and confrontation naming skills. The TOMM is included in the battery and serves the purpose of examining the validity of results obtained. A self-report measure that assesses memory complaints (verbal, visual, and total) is also completed by all patients.

Six cognitive measures and the Memory Complaints Inventory from the PNES neuropsychological battery were used for analysis. The Trauma Symptom Inventory-2 (TSI-2) was utilized in determining the diagnosis of PTSD along with clinical data. The Test of Memory Malingering (TOMM) and Wechsler Abbreviated Scale of Intelligence (WASI) were utilized as part of exclusion criteria demands.

2.2.1. TSI-2

The TSI-2 [34] is a 136-item self-report measure that is used to evaluate acute and chronic posttraumatic symptomatology in adults. The TSI-2 assesses for the effects of sexual and physical assault, intimate partner violence, combat, torture, motor vehicle accidents, mass casualty events, medical trauma, traumatic losses, and childhood abuse or neglect. The clinical scales of the instrument measure the extent to which the respondent endorses twelve trauma-related symptoms including the following: Anxious Arousal, Depression, Anger, Intrusive Experiences, Defensive Avoidance, Dissociation, Somatic Preoccupations, Sexual Disturbance, Suicidality, Insecure Attachment, Impaired Self-Reference, and Tension Reduction Behavior. The TSI-2 has been thoroughly examined with regard to reliability and validity. Predictive validity of PTSD using the TSI-2 was tested through discriminant function analysis using the T scores for the Anxious Arousal, Intrusive Experiences, and Defensive Avoidance scales. An optimally weighted combination of these TSI-2 scales significantly predicted PTSD with a sensitivity of 1.00 and a specificity of .88. In our study, we utilized the diagnostic TSI-2 standard composed of three scales to assess for PTSD: the Anxious Arousal (anxiety and autonomic hyperarousal), Intrusive Experiences (i.e., nightmares, flashbacks, upsetting memories), and Defensive Avoidance (cognitive and behavioral avoidance of distressing content) scales. These are in line with Criterion B (intrusive recollections), Criterion C (avoidant/numbing), and Criterion D (hyperarousal) of the DSM-IV.

The TSI-2 has two symptom validity subscales: Atypical Response (ATR) and Response Level (RL). According to the test manual, “administrations that produce RL T scores of 75 or higher should be considered invalid”, and “a raw score of 15 T>/= 100 indicates invalidity and is the recommended cutoff.”

2.2.2. TOMM

The TOMM [33] is a 50-item visual recognition test that is sensitive to motivation and effort and is specifically designed to differentiate between authentic memory impairments and malingering. The TOMM numerical scores combined with situational variables assist the neuropsychologist in making a clinical decision about the effort that is being put forth on testing. Patients who were excluded from the present study were determined to be exerting insufficient effort based on the recommendation stated in the Test of Memory Malingering (TOMM) professional manual; this includes the following: 1) a combination of numerical scores (i.e., Trials 1 and 2 of the TOMM), 2) behavioral observations suggestive of deficient effort, and 3) verification of an active pursuit of a personal injury suit or a disability petition.

2.2.3. WASI

The WASI [35] consists of four subtests: Vocabulary, Similarities, Block Design, and Matrix Reasoning. For the purpose of this study, FSIQ was utilized as a criterion for exclusion (FSIQ < 70).

2.2.4. Delis–Kaplan Executive Function System (D-KEFS)

The Delis–Kaplan Executive Function System (D-KEFS) [36] consists of 9 stand-alone tests used to evaluate higher level cognitive functions. The standard battery at our program includes two subtests: Trail Making and Color–Word Interference. Trail Making 4, a visual–motor sequencing task that requires alphanumerical shifting, and Color–Word Interference 3, a test that requires the inhibition of the automatic response of word-reading in favor of color naming, were included as cognitive variables.

2.2.5. Wechsler Memory Scale (WMS-III) [37]

The WMS-III consists of 11 subtests, with six primary subtests required to derive index scores. Logical Memory I and Logical Memory II assess immediate and delayed auditory verbal memory that is semantically organized. Raw scores were the cognitive variables in this study.

2.2.6. Continuous Visual Memory Test (CVMT) [38]

The CVMT comprises 112 complex, ambiguous drawings (e.g., polygons) and irregular nonsense figures that are presented in succession to the subject in 7 blocks of 16 stimuli. The 30-minute delayed multiple-choice recognition raw memory score was a cognitive variable in this study.

2.2.7. California Verbal Learning Test-II (CVLT-II) [39]

This is a list-learning test that assesses repetition learning, serial position effects, semantic organization, intrusions, and proactive interference. Delayed Spontaneous Recall raw score was a cognitive variable in this study.

2.2.8. Boston Naming Test (BNT) [40]

This is a test of visual confrontational word retrieval that consists of 60 line drawings in graded difficulty. The final score included in this battery is the raw score of spontaneous correct plus correct with semantic (but not phonemic) cues out of a total of 60.

2.2.9. Memory Complaints Inventory (MCI) [41]

The MCI is a self-report scale using a 5-item ("not at all" to "extremely") Likert scale to rate the severity of self-perceived memory problems. The 57 items are converted to 9 scales (General Memory Problems, Numeric Information Problems, Visuospatial Memory Problems, Verbal Memory Problems, Pain Interferes with Memory, Memory Interferes with Work, Impairment of Remote Memory, Amnesia for Complex Behavior, and Amnesia for Antisocial Behavior) and a Total of All Symptoms, with all scales ranging from 0 to 100% endorsement. The converted scores are compared with those of reference groups (e.g., Mild Head Injury, Severe Head Injury, "Normals Instructed to Fake Memory Impairment") to determine overendorsement of memory problems. For the purposes of this study, only Verbal Memory, Visuospatial Memory, and the MCI Total were analyzed.

2.3. Analysis

Analysis of variance (ANOVA) was used to determine the significance of differences between the three patient groups for the two demographic variables (age and years of education) and the cognitive measures. Cognitive measures included the following: Full Scale IQ (WASI), Verbal Fluency 4, Color–Word Interference 3 (D-KEFS), Logical Memory I and Logical Memory II (WMS-III), Delayed Recognition (CVMT), Delayed Spontaneous Recall (CVLT-II), and Total correct responses (BNT). Tukey's test was used for post hoc analyses of significant variables. Pearson chi-square tests between the 3 groups, with adjusted residuals used for post hoc analyses, were used for the analysis of demographic and medical factors with categorical variables. IRB approval for an anonymous archival record review was obtained with removal of non-relevant PHI (Copernicus IRB NRE1-11-155).

3. Results

Group 1 (patients diagnosed with PTSD) was composed of 17 women with mean age of 45.53 ± 10.74 and years of education of 14.06 ± 2.54. Group 2 (patients with trauma/no diagnosis of PTSD) was composed of 22 women and 7 men with mean age of 37.65 ± 11.86 and years of education of 13.88 ± 2.33. Group 3 (patients who denied a history of trauma) was composed of 17 women with mean age of 35.29 ± 12.1 and years of education of 14.35 ± 2.47. There was no significant difference between these variables or among duration of PNESs among the groups.

None of the patients in our sample earned scores on the TSI-2 validity scales that would require their elimination from the study. After comparing all neuropsychological variables among the three groups, Logical Memory II (delayed narrative memory) was significantly different between the 3 groups ($F = 3.65$, $p = .032$). Group 1 earned lower scores on LM II compared with the other two groups and earned significantly ($p = .024$) lower scores (8.69 ± 2.24) on this measure compared with Group 3 (10.82 ± 1.94). Analyses between the 3 groups on the 3 MCI scales that were examined showed significant differences for self-report on Verbal Memory ($F = 14.92$, $p = .000006$), Visuospatial Memory ($F = 4.16$, $p = .02$), and the MCI Total ($F = 11.1$, $p = .0001$). For all of the MCI measures, Group 1 scored higher (greater exaggeration) than Groups 2 and 3, which did not significantly differ from each other (Table 1).

When psychological and demographic factors were assessed, only 4 showed significant differences between groups, with Group 1 presenting with the highest rates compared with the other two groups. The three groups differed by the use of psychiatric medication, X^2 (2df, $N = 63$) $= 12.93$, $p < .002$; substance abuse, X^2 (2df, $N = 63$) $= 6.03$, $p = .049$; history of rape, X^2 (2df, $N = 63$) $= 9.12$, $p < .003$; and physical abuse X^2 (2df, $N = 63$) $= 5.73$, $p < .017$, with Group 1 presenting higher incidences of all (Table 2). The presence of traumatic head

Table 1
Cognitive variables of the sample with PNESs.

Tests	Group 1 (PTSD)			Group 2 (yes trauma, no PTSD)			Group 3 (no trauma)			F	p value
	N	M	SD	N	M	SD	N	M	SD		
WASI FSIQ	17	89.41	10.90	29	92.22	13.694	17	95.65	12.971	1	0.372
CVLT DR	15	7.87	4.26	29	9.59	3.627	17	8.41	3.337	1.29	0.283
CVMT DR	16	3.38	2.06	29	3.75	1.951	17	4	1.541	0.461	0.633
D-KEFS T4	15	7.13	2.92	29	8.97	2.927	17	7.12	4.136	2.47	0.093
D-KEFS CW3	13	8.46	3.23	29	6.94	3.549	16	7.75	3.568	0.94	0.397
BNT	15	50.73	4.03	29	48.45	10.049	17	47.53	8.931	0.58	0.565
WMS LM I	16	9.13	2.527	29	9.19	2.429	17	10.47	2.375	1.8	0.174
WMS LM II	16	8.69	2.243	29	9.72	2.439	17	10.82	1.944	3.65	0.032*

WASI FSIQ: Wechsler Abbreviated Scale of Intelligence Full Scale IQ, CVLT-II DR: California Verbal Learning Test-II Delayed Spontaneous Recall, CVMT DR: Continuous Visual Memory Test Delayed Recall, D-KEFS T4 and CW3: Delis–Kaplan Executive Function System Trail Making 4 and Color–Word Interference 3, BNT: Boston Naming Test, MCI: WMS-III LM:Wechsler Memory Scale-III Logical Memory.

* Significant at $p < 0.05$. With the exception of the WASI and MCI, all scores are raw scores.

Table 2
Historical variables of the sample with PNESs.

Yes/no	1 (PTSD)	2 (no PTSD)	3 (no trauma)	c2	p value
Psy meds	15/2	11/22	9/8	12.93	0.002*
Sub	13/4	2/28	0/17	6.026	0.049*
Sex Tr	13/4	10/22		9.115	0.003*
Phys Tr	13/4	31/19		5.728	0.017*
Loss Tr	9/8	12/20		1.081	0.299
Med Tr	5/12	4/28		2.118	0.416
Witness Tr	5/12	5/27		1.299	0.254
Psych Tr	5/12	7/25		0.341	0.559

Psy meds: psychopharmacological medications, Sub: substance abuse history, Sex Tr: trauma—sexual, Phys Tr: trauma—physical, Loss Tr: trauma—loss, Med Tr: trauma—medical, Witness Tr: Trauma—witness, Psych Tr: psychological trauma.
* Significant at $p < 0.05$.

injury ($p = 0.26$) was not found to be significantly different between groups.

4. Discussion

Results from this study showed that patients with PNESs/PTSD had significantly different (lower) verbal declarative memory function relative to patients with PNESs without PTSD on a test of narrative memory. Our sample's verbal memory results resemble those observed in PTSD (combat-related and sexual abuse-related), according to the growing body of literature on neuropsychological function in patients with PTSD who display similar and relative weaknesses in verbal declarative memory function compared with healthy subjects or with subjects with a history of trauma who have not gone on to develop PTSD [24,26,27]. It is interesting that a similarly significant difference was not detected between groups on another verbal memory measure (CVLT-II). These two measures differ in that the CVLT requires the learning of unrelated lists of words, albeit some can fit into certain semantic categories, while the LM subtests require the learning and coherent retelling of meaningful content. Patients with PTSD commonly find it challenging to present a clear narrative in therapy sessions. We might speculate that the Logical Memory subtests are exposing a particular cognitive weakness in these patients that a list-learning task does not identify (Table 1).

Memory disturbances are predominant in the presentation of PTSD, in the form of frequent complaints of everyday memory problems with emotionally neutral material. Our patients with PNESs/PTSD self-assessed their memory functions (Total, Verbal, and Visual) to be extremely impaired, much more so than the group without PTSD did regardless of trauma history (Table 3). These self-assessments by patients with PNESs/PTSD were consistent with statistically lower scores on standardized testing of verbal memory, although not with visual memory scores.

The group with PNESs/PTSD in the current study reported more common histories of substance abuse than the rest of the sample with PNESs, similar to previous reports of patients with PTSD [42,43]. In addition, the greater use of psychopharmacological agents found in our group with PNESs/PTSD might indicate a higher level of psychological distress and symptoms in this group. The presence of higher instances of sexual and physical abuse (interpersonal trauma) in our sample with PNESs/PTSD compared with our patients without PTSD is consistent with trauma disorder development.

There are reports in the literature of patients with PNESs performing below normal limits on neuropsychological testing compared with standardized norms and with patients diagnosed with epilepsy [1,30,44,45], although no specific deficit pattern has been identified in PNESs. However, when we examined the sample based on the psychiatric diagnosis of PTSD, we identified relative cognitive weaknesses which were different than those seen in other patients with PNESs alone and were more similar to the verbal memory patterns reported in the literature for PTSD alone. In fact, patients with PNESs/PTSD differed significantly from the other patients with PNESs on objective and subjective memory scores. In contrast with other reports [41], we did not find that duration of PNESs or other historical data explained this poorer memory function.

Relatively weaker verbal memory found in patients with PNESs/PTSD compared with the other subjects with PNESs is clinically significant in that lower episodic verbal memory can influence treatment outcome. In fact, Wild and Gur [46] identified that PTSD non-responders to cognitive behavioral treatment (CBT) had significantly poorer performance on measures of verbal memory compared with PTSD responders and demonstrated narrative encoding deficits. Therefore, verbal memory deficits may diminish the effectiveness of traditional cognitive-based treatment and should be considered when deciding on treatment options. Moreover, our finding that verbal memory deficits in patients with PNESs/PTSD more closely resemble cognitive patterns in patients with PTSD alone indicates that empirically supported treatment for PTSD [i.e., exposure therapy, cognitive processing therapy (CPT), and eye movement desensitization and reprocessing (EMDR)] should be considered for this subgroup [47].

There are two important elements that were included in this study with the purpose of strengthening its design. It has been suggested that cognitive deficits found in many patients with PNESs and PTSD are in fact due to insufficient effort (malingering) [31] being put forth. The American Academy of Clinical Neuropsychology [28] recently published a position paper in which the importance of including testing of effort in neurocognitive test batteries was indicated. It is for this reason that our study took this into account and controlled for the possibility of memory malingering by excluding patients using the TOMM and concordant behavioral observations. Moreover, because a history of a traumatic brain injury could also have had an effect on the cognitive measures being used, the presence or absence of this type of injury was considered and was not found to explain the cognitive differences seen in our sample.

Because this study utilized several measures, conclusions should be circumspectly drawn since multiple comparisons increase the potential for a type-I error. However, these 7 measures are unrelated and do not have multicollinearity, and, so, they would not significantly correlate with each other. A second limitation is that our sample is missing those patients who were diagnosed with PNESs through video-EEG monitoring but did not complete neuropsychological testing because

Table 3
Trauma Symptom Inventory-2 and Memory Complaints Inventory scores.

Tests	Group 1 (PTSD)			Group 2 (yes trauma, no PTSD)			Group 3 (no trauma)			c2	p value
	N	M	SD	N	M	SD	N	M	SD		
TSI-2 Anxious Arousal	16	72.50	6.143	29	58.38	8.715	16	56.00	11.069		
TSI-2 Intrusive Experience	16	70.69	9.816	29	56.72	12.750	16	49.69	10.769		
TSI-2 Defensive Avoidance	16	67.44	9.187	29	57.72	9.602	16	50.13	10.327		
MCI Verbal	17	70.29	22.74	29	30.17	23.470	17	36.88	28.68	14.92	0.000**
MCI Visual	17	45.88	22.52	29	27.27	24.195	16	25.63	23.15	4.16	0.02*
MCI Total	16	53.94	20.93	28	26.57	19.778	15	23.13	17.59	11.1	0.0001**

TSI-2 = Trauma Symptom Inventory-2 and MCI = Memory Complaints Inventory.
* Significant at $p< 0.05$
** Significant at $p< 0.01$

they left our practice after receiving the diagnosis. This group of patients could have different, clinically relevant characteristics, but it was not possible to examine them. In addition, we did not collect data on ethnic and racial backgrounds of patients, and important information regarding cultural variations in PNES pathology and neuropsychological functions may have been overlooked.

Future studies exploring the neurobiological underpinning of PNESs within certain types of psychopathologies (i.e., PTSD) can further clarify the growing body of evidence of differential subgroups within the overarching classification of PNESs. Along similar lines, measurement of PTSD symptom severity could add to our understanding of these patients. From a treatment perspective, it will be necessary to examine treatment response in patients diagnosed with PNESs and PTSD with diagnostic-specific treatments (i.e., prolonged exposure—PE or eye movement desensitization and reprocessing—EMDR) compared with general psychological treatments (cognitive behavioral treatment).

In sum, identifying a distinctive diagnostic category such as PTSD supported through cognitive and psychological testing and clinical interview within the general PNES classification is important from a diagnostic and treatment perspective. The present findings provide an indication that cognitive patterns of patients with PNESs/PTSD more closely resemble those of patients with PTSD alone compared with others who have PNESs alone and, therefore, may gain greater benefit from empirically validated PTSD treatment rather than from other less specific treatments.

Conflict of interest

The authors have nothing to disclose and vouch that this is an original paper that has not been submitted elsewhere.

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