Gender-Related Differences in Semiology of Psychogenic Non-Epileptic Seizures

H. Sabiha TÜRE¹ , Işıl TATLIDİL¹ , Esin KILIÇARSLAN² , Galip AKHAN¹

¹Neurology Department, İzmir Katip Çelebi University Atatürk Education and Research Hospital, İzmir, Turkey

²Psychiatry Department, İzmir Katip Çelebi University Atatürk Education and Research Hospital, İzmir, Turkey

ABSTRACT

Introduction: The aim of the study is to detect possible gender-related differences in the semiology of psychogenic non-epileptic seizures (PNES).

Methods: One hundred fifty-five patients (male: female=63:92) aged 13 to 67 years, who were diagnosed with PNES by video-monitoring electroencephalogram (EEG) between 2010 and 2017, were included in this retrospective study. Patients were grouped according to their gender. The primary semiological characteristics of PNES for each case were defined, standardized, and categorized by an epileptologist during video-monitoring EEG. The chi-square test and the Fisher exact test were used statistically.

Results: An age histogram showed peaks at ages 20 to 23 and at ages

40 to 43, which were more prominent in the female gender. Whereas major motor activity ($p=0.032$), lateralizing motor activity ($p=0.017$), and opisthotonic posture and pelvic thrust motion ($p=0.017$) were significantly related to the male gender, weeping ($p<0.001$) was significantly related to the female gender.

Conclusion: Our study showed that there are some semiological differences between the genders in PNES. In male patients, lateralized motor findings are more prominent and not accompanied by ictal crying in seizures, which may lead to further confusion with epileptic seizures. It is important to know the semiological characteristics for early and accurate diagnosis.

Keywords: Psychogenic non-epileptic seizures, semiology, gender

Cite this article as: Türe HS, Tatlıdil I, Kılıçarslan E, Akhan G. Gender-Related Differences in Semiology of Psychogenic Non-Epileptic Seizures. Arch Neuropsychiatry 2019;56:178-181.

INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are a type of somatoform disorder consisting of paroxysmal episodes resembling epileptic seizures (ES) without concomitant electroencephalographic (EEG) activity (1). Distinguishing PNES from ES is important to avoid the overdiagnosis of epilepsy and overtreatment of patients believed to have epilepsy (2). A detailed questioning about seizure characteristics while taking the patient history is important for the differential diagnosis of ES and PNES in clinical practice (3). Video-monitoring EEG, which is the gold standard for PNES diagnosis, is a good method for analyzing the semiological characteristics of both ES and PNES (1-3).

The dissimilarity between the genders in PNES is a remarkable subject to consider. The prevalence rate of PNES is approximately three times higher in females than in males (4, 5). The reason for the dominance of the female gender has not yet been clarified. However, both genders have some differences in terms of concomitant social conditions and underlying psychopathological disorders. Recent studies suggest that male patients diagnosed with PNES have lower rates of history of sexual or physical abuse, previous psychiatric diagnosis, somatic complaints, and employment, as well as higher rates of emotional maladjustment, than females diagnosed with PNES (6-8). On the other hand, according to

another recent study, PNES in males is more likely to be underdiagnosed, compared with females, in outpatient clinics (9). It has been thought that semiological differences, physicians' attitudes, the bias caused by the knowledge of the relationship between the female gender and PNES, and differences in risk factors between the genders could cause this situation (8, 9). Despite many asymmetries in etiology and different demographics, few differences in semiology have been shown, according to several previous studies. Whereas a long duration, weeping, atonic posture, and stiffening are more frequent in the female gender, major motor activities such as generalized tonic-clonic movements are more frequent in males (6, 8, 10-12). It is worth mentioning that not all studies showed the same significant relationship between the genders in the aforementioned parameters. Low numbers in the studies, different ways of classifying non-epileptic seizures, and the local sociocultural differences may be the cause of the different results in the studies. Moreover, the asymmetrical distribution of PNES between the genders may cause a failure to show some statistically significant results. We hypothesized that there could be some differences in terms of the characteristics of the semiology of PNES between the genders and that the differences may cause underdiagnosis of PNES in the male population.

Correspondence Address: H. Sabiha Türe, İzmir Katip Çelebi University Atatürk Education and Research Hospital, Neurology Department, İzmir, Turkey • **E-mail:** sabihature@yahoo.com

Received: 08.10.2018, **Accepted:** 20.03.2019, **Available Online Date:** 16.07.2019

©Copyright 2019 by Turkish Association of Neuropsychiatry - Available online at www.noropskiyatriarsivi.com

MATERIALS AND METHODS

Subjects

Patients who were diagnosed with PNES by video-monitoring EEG in our clinic between 2010 and 2017 were included in this retrospective study. Each seizure observed by video EEG was analyzed by an epileptologist, and common characteristics of non-epileptic seizures were defined and categorized according to the activity during the seizure. The patients were grouped according to gender.

The protocol was carried out in accordance with the ethical standards of the Declaration of Helsinki, and the local ethics committee reviewed and approved the study protocol. All patients had given their written informed consent before video EEG monitoring.

Semiology

First, we classified non-epileptic seizures according to their common features, including akinetism-swooning-syncope-like state and major motor activity. Those two parameters included most of the cases. If a person had an akinetism-swooning-syncope-like state, (s) he could not have major motor activity and vice versa. Still, there were some cases that could not be classified into either category. Those included some types of paroxysm such as auras and subjective symptoms or weeping.

Major motor activity: These seizures included mostly proximal extremity movements such as shaking, stiffening, or a dystonia-like state, tremors, tonic-clonic-like movements, side-to-side head movements, and hypermotor seizure-like movements. In this group, conscious and unconscious as well as unilateral and bilateral movements were involved.

Akinetism-swooning-syncope-like state: These seizures included a state of akinetism, a syncope-like-state, or sudden loss of muscle tone. For the most part, there were no proximal extremity motions. Hyperventilation, moaning, weeping, changes of facial expression, and fine movements in the distal part of the extremities, feet, and hands, were included.

Cases were classified according to some seizure characteristics that may be confused with epileptic seizure, such as lateralizing movements and a postictal-like state.

Lateralizing movement referred to one-sided movements or motion that made the neurologist consider central localization. One-sided hypermotor-like movements, one-sided tonic-clonic-like movements, one-sided dystonia, head or eye deviation, with the exception of upward or downward deviation, and one-sided facial twitching were included.

Postictal-like state: Defined as the time interval that some patients experienced between ictal-like activity and a normal conscious state.

The common characteristics making the diagnosis of PNES obvious were also determined, including weeping, opisthotonic posture or pelvic thrusting, giving response-communicating, and eye closure.

Hyperventilation, auras, and other subjective feelings were also determined to be semiological features commonly seen in the population.

Because epileptic seizures longer than 5 minutes are considered to be status epilepticus, a serious clinical situation that must be seen in the emergency department, prolonged duration of the seizure could be ruled as PNES, whereas seizures of shorter duration could be confused with ES. For this reason, the duration of seizure was dichotomized as greater than 5 minutes and 5 minutes or less. Because trauma ($n=3$), urinary and fecal incontinence ($n=0$), and tongue biting ($n=0$) have not been or are seldomly seen in our PNES population, we did not include those features of semiology in this study.

Statistical Analysis

Statistical analysis of the study data was performed on SPSS (Statistical Package for Social Sciences) Windows 15.0 software. The chi-square test and Fisher exact test were used to make comparisons between independent groups on variables of semiological characteristics. A p value less than 0.05 was considered significant.

RESULTS

Demographic Data

One hundred fifty-five patients (male:female=63:92) aged 13 to 67 years who were diagnosed with PNES were analyzed. The mean patient age was 33.96 years ($SD \pm 12.14$), 33.90 years ($SD \pm 11.34$) for males and 34.00 years ($SD \pm 12.72$) for females (Table 1). The age histogram showed two peaks at ages 20 to 23 and 40 to 43, which were more prominent in the female gender. Thirty-five (22.6%) had confirmed concomitant epilepsy (based on their video EEG monitoring and clinical history). Twenty patients (12.6%) had a family history of epilepsy. No significant difference between the genders has been found in background data in terms of accompanying epilepsy diagnosis and family history of epilepsy (respectively $p=0.252$ and 0.305).

Semiological Features

There were a few relationships between defined semiological characteristics and gender. Major motor activity, one of the common characteristics of PNES, was significantly related to the male gender ($p=0.032$). Statistical results for akinetism-syncope-like seizures and seizures with auras and subjective feelings showed no significant differences between the genders. The duration cutoff of 5 minutes showed no significant differences between the genders. As to statistics of semiological characteristics, major motor activity ($p=0.032$), pelvic thrusts and opisthotonic posture ($p=0.017$) and lateralizing motion ($p=0.027$) showed a significantly high correlation with the male gender, whereas weeping was significantly related to the female gender ($p<0.001$). There was no significant relation with other defined semiological characteristics of seizures, such as giving response during seizure, eye closure, hyperventilation, and the existence of a postictal-like state, between the genders.

Table 1. Descriptive statistics of age for each gender and general population

	Women n: 92 (59.4%)	Men n: 63 (40.6%)	All patients n: 155	P value
minimum	15	13	13	0.197
maximum	65	67	67	
SD $\pm$	12.72	11.34	12.14	
Mean	34.00	33.90	33.96	

SD, standart deviation.

Table 2. Semiological variables of PNES for males and females

	Women (%)	Men (%)	P value
Seizure Duration (>5 minute)	55.4	55.5	0.988
Major motor activity	54.3	71.4	0.032
Akinetism-syncobe	34.7	20.6	0.57
Auras-subjective feelings	29.3	20.6	0.223
Giving response-communicating	34.7	22.2	0.093
Eye closure	56.5	68.2	0.141
Hyperventilation	39.1	33.3	0.462
Opisthotonic and pelvic thrust motion	7.6	20.6	0.017
Weeping	20.6	0.0	<0.001
Postictal-like state	17.3	15.8	0.804
Lateralizing motion	14.1	28.5	0.027

DISCUSSION

According to our results, the male patient percentage (40.6%) was slightly higher than in other studies in the literature. As the ratio is 2:3 (male: female), which is still in favor of female dominance, our ratio is high compared with those in previous studies, which are between 1:2 and 1:3 (2, 4–6, 8, 10–12, 13). The high frequency of presentation of PNES in patients at ages 40 to 43 was also remarkable. Pooya et al. hypothesized that the demographics of the PNES population show slight differences between different cultural groups (10). It is also valid for our study. Nonetheless, there are still some differences that may be affected by sociocultural background. The peak ages of presentation, 20 to 23 years and 40 to 43 years in our study, may be partly related to the common social issues of the population concerning the certain age groups. Still, the high frequency of PNES at ages 35 to 40 in the male population is a surprising finding that could not be directly explained by social issues.

Demographic, clinical, etiological, and physiological differences have been reported in patients with PNES according to gender in the literature. (10–13). However, most of the research data tends to be statistically inadequate, due to very unequal distribution among the genders because of the reasonably lower proportion of the male population. In our study, the ratio of male patients was higher than in the literature, and there were some gender-related clinical semiological differences in PNES patients. Whereas major motor activity, pelvic thrust and opisthotonic posture, and lateralizing motion were significantly more frequent in males than in females, weeping was significantly more frequent in the female population.

The high frequency of major motor activity in the male population and the high frequency of weeping in the female population has been reported in the literature recently. Gale et al. and Merode et al. showed that major motor activity or violent actions were seen significantly more frequently in the male population, which was described as the “male way of acting out distress” (11, 14). Oto et al. also showed a higher frequency of weeping in the female population after seizures (6). Whereas weeping is an accepted way for the female population to express emotions, weeping is unacceptable for the male population in the society, which may cause the difference.

A high frequency of pelvic thrust movements, opisthotonic posture, and lateralizing movements in male patients differs from the literature. Alessi et al. showed that pelvic thrust movements were significantly rare in the pediatric population compared with adults (15). Social unacceptability of the motion for the female gender may cause the low frequency of opisthotonic posture in female patients. From another point of view, pelvic thrusting and opisthotonos is a semiological characteristic more typical for PNES than epilepsy (3) that, together with weeping, which is also typical for PNES, aids the diagnosis of PNES in clinical practice. On

the other hand, lateralizing movements during seizure are primarily in favor of an ES diagnosis, which may cause the misdiagnosis of epilepsy in the population. Considering the fact that male PNES cases tend to be underdiagnosed in clinical practice, the high frequency of lateralizing motion in the male gender could be one of the reasons (3). Say et al. found a longer ictal duration in a pediatric female population (12). Korucuk et al. found that the duration of seizures was significantly longer in women, but they did not find any semiological differences between the genders (16). In our study, no significant difference was found in terms of seizure duration (>5 minutes) between the genders.

From another point of view, differences in semiology between the genders could be influenced by different demographics such as level of education, cultural differences, nationality, etc., which may be unequally distributed between the genders. In a study in which the level of education was correlated with the clinical picture of PNES, the level of education did not have a significant effect on the clinical picture of PNES (17). On the other hand, comparing characteristics of PNES between patients from the US and Brazil, another study suggested that patients from the US had more seizure types and more often reported subjective seizures (18). Despite all of our patients being from Turkey, there still could be some subcultures whose clinical pictures of PNES might vary.

Despite a large amount of similarities of PNES between the genders, some differences have also been shown. However, the underlying causes of both the large similarities and the small differences remain unclear. Some biological mechanisms may explain the reasons for the large similarities. According to a previous study by Labate et al., it is suggested that motor and premotor regions in the right hemisphere and the cerebellum bilaterally play an important role in the pathogenesis of PNES. It was hypothesized that there could be a multistep model where PNES phenomenology is driven by the psychological factor interacting with specific biologic abnormalities (19). Mcsweeney et al. examined patients with PNES radiologically and found that cortical thickness increase in motor, sensory, and occipital regions and cortical thickness decreased in temporal and frontal brain regions in patients with PNES compared to controls. However, they did not find evidence of atypical gyrification, suggesting abnormalities of cortical development and organization in prenatal and early childhood (20). The contradictory findings in the literature probably reflect the etiology and phenomenological heterogeneity of PNES, and this also affects PNES semiological findings.

Our study has some limitations. First, because it is a retrospective study and we do not have reliable data about the accompanying psychopathologies of the patients, the accompanying psychopathologies were not assessed as a parameter affecting semiology. Further, it has been shown in previous studies that accompanying psychopathologies in the genders are also different. Therefore, the underlying psychopathologies

may also have some effects on PNES semiology (6). Second, it is a single-center study and may not represent the whole spectrum of PNES cases.

CONCLUSION

Our study has shown some differences of semiology of PNES between the genders. Taking them into account along with the history of a patient investigated for the differential diagnosis of epilepsy could be helpful in the detection of PNES. The presence of lateralized findings and the absence of ictal crying could cause more epileptic-like non-epileptic seizures, which may lead to long-term, unnecessary antiepileptic treatment with the misdiagnosis of epilepsy. Our study showed that these findings are more common in male PNES patients. It should be kept in mind that PNES characteristics may differ between the genders and may be confused with epileptic seizures, especially in male patients.

Acknowledgements: The Authors thank Assoc. Prof. Dr. Ferhan Elmalı for his help in statistical analysis.

Ethics Committee Approval: The protocol was carried out in accordance with the ethical standards of the Declaration of Helsinki, and the local ethics committee reviewed and approved the study protocol.

Informed Consent: All patients had given their written informed consent before video EEG monitoring.

Peer-review: Externally peer-reviewed.

Author contributions: Concept – HST, GA; Design – HST, GA; Supervision – HST; Resource – GA; Materials – HST, EK; Data Collection &/or Processing – HST, EK; Analysis &/or Interpretation – HST, EK; Literature Search – IT, HST; Writing Manuscript – HST, IT; Critical Review – HST, GA.

Conflict of Interest: There is no conflict of interest.

Financial Disclosure: None

REFERENCES

1. Avbersek A, Sisodiya S. Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures? *J Neurol Neurosurg Psychiatry* 2010;81:719–725. [CrossRef]
2. Asadi-Pooya AA. Psychogenic nonepileptic seizures: a concise review. *Neurol Sci* 2017;38:935–940. [CrossRef]
3. LaFrance WC Jr, Ranieri R, Blum AS. Nonepileptic seizures - objective phenomena. *Handb Clin Neurol* 2016;139:297–304. [CrossRef]
4. Sigurdardottir KR, Olafsson E. Incidence of psychogenic seizures in adults: a population-based study in Iceland. *Epilepsia* 1998;39:749–752. [CrossRef]
5. Szaflarski JP, Ficker DM, Cahill WT, Privitera MD. Four-year incidence of psychogenic nonepileptic seizures in adults in Hamilton county. *Neurology* 2000;55:1561–1563. [CrossRef]
6. Oto M, Conway P, McGonigal A, Russell AJ, Duncan R. Gender differences in psychogenic non-epileptic seizures. *Seizure* 2005;14:33–39. [CrossRef]
7. Dworetzky BA, Strahonja-Packard A, Shanahan CW, Paz J, Schauble B, Bromfield EB. Characteristics of male veterans with psychogenic nonepileptic seizures. *Epilepsia* 2005;46:1418–1422. [CrossRef]
8. Thomas AA, Preston J, Scott RC, Bujarski KA. Diagnosis of probable psychogenic nonepileptic seizures in the outpatient clinic: does gender matter? *Epilepsy Behav* 2013;29:295–297. [CrossRef] <https://doi.org/10.1016/j.yebeh.2013.08.006>
9. Noe KH, Grade M, Stonnington CM, Driver-Dunckley E, Locke DE. Confirming psychogenic nonepileptic seizures with video-EEG. *sex matters. Epilepsy Behav* 2012;23:220–223. [CrossRef]
10. Asadi-Pooya AA, Emami M, Emami Y. Gender differences in manifestations of psychogenic non-epileptic seizures in Iran. *J Neurol Sci* 2013;332:66–68. [CrossRef]
11. Gale SD, Hill SW, Pearson C. Seizure semiology in males with psychogenic nonepileptic seizures associated with somatic complaints. *Epilepsy Res* 2015;115:153–157. [CrossRef]
12. Say GN, Tasdemir HA, Ince H. Semiological and psychiatric characteristics of children with psychogenic nonepileptic seizures: Gender-related differences. *Seizure* 2015;31:144–148. [CrossRef]
13. Myers L, Trobliger R, Bortnik K, Lancman M. Are there gender differences in those diagnosed with psychogenic nonepileptic seizures? *Epilepsy Behav* 2018;78:161–165. [CrossRef]
14. Van Merode T, De Krom MCTFM, Knottnerus JA. Gender related differences in non-epileptic attacks: a study of patients in the literature. *Seizure* 1997;6:311–316. [CrossRef]
15. Alessi R, Vincentiis S, Rzezak P, Valente KD. Semiology of psychogenic nonepileptic seizures: Age related differences. *Epilepsy Behav* 2013;27:292–295. [CrossRef]
16. Korucuk M, Gazioglu S, Yildirim A, Karaguzel EO, Velioglu SK. Semiological characteristics of patients with psychogenic nonepileptic seizures: Gender-related differences. *Epilepsy Behav* 2018;89:130–134. [CrossRef]
17. Asadi-Pooya AA, Bahrami Z. Education in patients with psychogenic nonepileptic seizures. *Seizure* 2019;64:74–76. [CrossRef]
18. Asadi-Pooya AA, Valente K, Alessi R, Tinker J. Semiology of psychogenic nonepileptic seizures: An international cross-cultural study. *Epilepsy Behav* 2017;75:210–212. [CrossRef]
19. Labate A, Cerasa A, Mula M, Mumoli L, Gioia MC, Aguglia U, Quattrone A, Gambardella A. Neuroanatomic correlates of psychogenic nonepileptic seizures: a cortical thickness and VBM study. *Epilepsia* 2012;53:377–385. [CrossRef]
20. Mcsweeney M, Markus Reuber M, Hoggard N, Levita L. Cortical thickness and gyrification patterns in patients with psychogenic non-epileptic seizures. *Neurosci Lett* 2018;678:124–130. [CrossRef]