Functional seizures are not less important than epilepsy

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ABSTRACT

Functional seizures (FS) are frequently encountered in neurology clinics, often affect young adults, and have significant negative impacts on many aspects of a person's life. In the current narrative review, we searched the literature regarding some of the consequences of FS (i.e., psychiatric comorbidities, social consequences, costs that are associated with the condition, cognitive impairment in patients with FS, the quality of life of the people with FS, and the increased risk of mortality that is associated with FS). Evidence shows that FS have significant negative consequences, comparable in their magnitude to those affecting patients with epilepsy. The clinical and scientific communities should take steps to address these consequences through clinical care and research that prioritizes, facilitates, and expedites evidence-based diagnosis and treatment for FS.

Contents

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1. Introduction

Functional seizures (FS), also known as psychogenic nonepileptic seizures (PNES) or dissociative seizures (DS), are characterized by paroxysmal events that semiologically may look like

epileptic seizures, but are not due to an underlying epileptic activity. Hence, the electroencephalogram does not show ictal epileptiform discharges. FS are instead thought to be caused by a complex set of interrelated psychological, social, and biological factors, and are often associated with psychological stressors [1,2]. This condition is frequently encountered in neurology clinics [3], often affects young adults and has significant effects on many aspects of a person's life [4].

In the current narrative review, we searched the literature regarding some of the consequences of FS, including psychiatric comorbidities, social consequences, financial costs associated with the condition, quality of life of the patients, and the increased risk of mortality that is associated with FS. We aimed to highlight and underscore the significance of FS in a concise and evidence-based manner.

2. Psychiatric comorbidities

People with FS are at higher risk for psychiatric comorbidities compared to the general population; this is comparable with that in the people with epilepsy [5–7]. Co-existing psychiatric disorders have a complex and intricate relationship with FS. They may represent a predisposing risk factor, a precipitant, an underlying cause, or a consequence of this chronic and disabling disorder [5–7]. While there are many similarities between patients with FS and those with functional movement disorders [8], people with FS have greater levels of depressive and anxiety symptoms, more frequent history of sexual abuse, greater levels of alexithymia, higher levels of dissociative symptoms, and distressing traumatic events occurring at an earlier age compared to those in people with functional movement disorders [9].

Depression is the most common psychiatric disorder among people with FS, with an average prevalence of 31% and cumulative lifetime rates ranging from 36% to 80% [6,10]. Depression occurs more often among people with FS than in the general population [11] or among people with epilepsy [10,12]. Remarkably, people with FS may not show the spectrum of symptoms that are typically associated with clinical depression. In a systematic review conducted by Walsh and colleagues [10], five studies used the Personality Assessment Index and showed that people with FS reported more physical difficulties than people with epilepsy. Therefore, people with FS may more frequently experience and report physical symptoms of depression and somatic expressions of distress rather than the cognitive or emotional aspects of depression; this may lead clinicians to overlook depression in this patient population [10,13]. Furthermore, depression may explain more variation in quality-of-life inventories among people with FS than seizure-related factors [14,15]. Depression may also predict the level of dysfunction experienced by these patients [12,14–18].

The prevalence of anxiety disorder among people with FS differs significantly in various studies (from 9% to 71%), because of the different methodologies and also the complexity of the clinical presentations of anxiety disorders (e.g., panic attacks, generalized anxiety disorder) [7]. In a systematic review and meta-analysis, the reported rate of panic attacks in FS ranged from 17% to 83%, with physical symptoms more commonly reported, and affective symptoms less so. 'Dizziness or light-headedness' was more frequent than 'fear of dying' in people with FS (68% *vs.* 23%) [19]. Of note, panic may play a role in FS characteristics as a response to heightened arousal in the absence of raised anxiety levels [20]. The increased autonomic arousal in FS [21] and the use of hyperventilation – a cardinal feature of panic attacks - to provoke FS support this hypothesis [22].

People with FS report higher rates of early life traumatic experiences than people with drug-resistant epilepsy [23]. Since

trauma plays an important etiological role in many cases of FS, it is not surprising that the prevalence of post-traumatic stress disorder (PSTD) among people with FS is high, ranging from 38% to 64% [24,25]. People with FS who had experienced traumatic events especially in their childhood tend to present more dissociative experiences, more psychiatric comorbidities (i.e., depression and anxiety), and a lower quality of life than those without a history of traumatic experiences [26–28].

People with FS may also suffer from comorbid personality disorders (e.g., borderline personality disorder) [11] and increased rates of suicide [29]. Neurologists must be aware of these patients' characteristics to provide support after the diagnosis of FS is made, preventing the devastating and at times fatal outcomes that may be associated with this condition (e.g., injuries, social problems, suicide, etc.). Beyond the direct consequences of FS, psychiatric comorbidities may impair the patients' functioning. Therefore, the added consequences of these comorbidities must be promptly recognized and treated as a priority to improve the quality of life of the people with FS.

3. Social consequences

Across nations and cultures, people who suffer from FS, continue to report detrimental effects on social aspects of their lives [4,30]. Studies have shown that across different nations and continents, people with FS have low rates of employment (approximately 1 in 3) and high rates of dependence on state-provided disability payments (where they are available to them) compared with the general populations [31–33]. The partners of people with FS may also experience higher rates of underemployment and social transfer payments than matched controls [4]. In addition, only a minority (about one-fifth) of adults with FS reported driving a motor vehicle in their routine daily lives [34] and driving restriction is a commonly endorsed barrier to socializing and accessing healthcare by these patients [35]. Furthermore, learning problems and educational difficulties are common among people with FS [36–38]. The associations between FS and education have been interpreted in two ways: 1) educational problems and learning disabilities may interact with other risk factors (e.g., adverse childhood experiences) to increase the risk for development of FS, and 2) reduced educational achievement may result from the onset of FS [39]. Finally, people with FS may experience problems in their marriage quality and marital outcomes [39,40].

Social aspects of life are important determinants of health and quality of life (QOL). Therefore, since FS have debilitating effects on patients' lives, they are frequently associated with a decreased QOL in these patients [39], even worse than that in people with epilepsy [14,41,42]. In addition, the caregivers' QOL scores in people with FS are comparable to those of caregivers for people with epilepsy [43]. Also, the employment rates, educational levels, driving rates, and marital status of people with FS are comparable with those in people with epilepsy (or may even be worse in people with FS) [14,39,40,43,44]. In brief, the detrimental social effects and burden of FS on individual patients, their caregivers, and the society at large, are comparable to those in people with epilepsy. We should emphasize that some of these detrimental social effects of FS may be inevitable in the light of the regulations or the greater societal good that needs to be placed over the good and well-being of an individual (e.g., driving restrictions). These issues should be addressed in future studies.

4. Impaired cognition

Mood and objective cognitive function are both important contributors to subjective cognitive function [45]. While people with

FS may complaint from impaired cognition (more than that by healthy controls), their cognitive impairment is usually not as bad as that in patients with epilepsy [46–48]. Nonetheless, cognitive impairment in patients with FS have potentially important clinical implications [49]. Cognitive impairment may lower the ability of patients to process and adjust to their emotional states appropriately [50]. In one study, people with FS showed improved cognition at one year of follow-up, particularly in language and executive functions. This implies the potential benefits of an early and accurate diagnosis, which may range from improved cognition to better management [48]. Cognitive function should be evaluated in all patients with FS and cognitive impairment should be considered in planning the neuropsychological rehabilitation of these patients [49].

5. Costs

Before the correct diagnosis has been established, people with FS usually receive treatment with antiseizure medications (ASMs) resulting in higher health care utilization and costs [51]. Multiple visits to the emergency departments, hospital admissions, outpatient visits, and extensive, repetitive, and often unnecessary diagnostic investigations (EEG, neuroimaging, and laboratory blood tests) can further increase the direct costs related to FS. In one study, the health care utilization and costs prior to and after the diagnosis of FS were calculated. The cost associated with FS during 12 months before the diagnosis was $4567 ± $4329 USD per person; this cost was $2783 ± $3404 USD during 12 months after the diagnosis (a reduction of nearly $1800 per person) [51]. A small but rapidly growing body of studies have evaluated the economic impacts on health resource utilization and costs that are associated with FS [51–55]. These studies generally utilized retrospective designs with different study periods and evaluating various outcomes. The comparability of the results across these studies is hampered by the differences in itemization and calculation of the costs, healthcare systems, and temporal variability of the costs [55]. Despite these limitations, resource utilization cost studies have shown that FS represent a considerable source of healthcare costs [51–55]. The higher resource utilization is mainly related to a longer duration of FS due to misdiagnosis or delayed diagnosis. All studies in this field have consistently shown that ensuring confirmation of FS by video-EEG monitoring significantly reduces the costs associated with erroneous or delayed diagnosis of the condition [54–56].

Remarkably, most studies have focused on the direct costs that are associated with FS (i.e., healthcare resource utilizations, including hospitalization, outpatient visits, diagnostic investigations, physiotherapy, and use of medications). Only one study investigated the (indirect) social costs, related to welfare benefits and reduced work productivity with consequent loss of market income [4]. People with FS and their partners received welfare benefits (including subsistence allowances, disability pensions, social security and assistance) more frequently than controls. Furthermore, people with FS had lower levels of employment and lower earned income up to three years before the diagnosis [4].

Overall, there is consistent evidence from the literature indicating that FS are associated with a considerable direct and indirect economic burden on the health care systems, comparable to that associated with drug-resistant epilepsy [55]. Establishing an early diagnosis strategy is effective in minimizing undue healthcare resource utilization, and health and social costs. Although one preliminary study showed that intensive short-term dynamic psychotherapy can be cost-effective [57], further studies to evaluate the impact on healthcare costs of specific treatments for FS are required.

6. Quality of life

Functional seizures often have debilitating effects on patients' lives. A systematic review of health-related quality of life (QOL) in adults with FS concluded that the majority of studies on this issue were cross-sectional and of weak to moderate quality (14 articles were included for the review in 2015) [58]. However, there is consensus that many patients with FS have impaired QOL (comparable to those with epilepsy) [59,60]. In a recent study, the investigators observed more psychiatric comorbidities with poorer QOL in people with FS compared with those in patients with drug-resistant epilepsy [61]; this corroborates another recent study in which the authors observed that people with FS scored significantly higher in anxiety and depression scales and had lower levels of QOL compared with patients with epilepsy [42]. Other similar studies have provided the same evidence (of a poorer QOL in people with FS compared with that in patients with epilepsy) [62]. Depression (the strongest correlate), dissociation, somatic symptoms, impaired cognition, and family dysfunction are often negatively associated with health-related QOL in people with FS [41,58,63].

In clinical practice, outcome of FS is usually discussed in terms of seizure reduction; however, the relevance of FS reduction to QOL improvement is questionable [41,58]. Psychological and interpersonal factors are more importantly related with the QOL and these issues should be considered in the management process of people with FS [58]. The current existing evidence strongly suggests that mental health care may improve the QOL of people with FS [64].

7. Mortality

FS are known to be highly disabling [58]. There is now an emerging body of evidence suggesting that people with FS also have increased rates of mortality compared to healthy controls; this rate is comparable to mortality rates among people with epilepsy [4,65,66].

Historically, clinicians have documented numerous individual cases of iatrogenic mortality resulting from efforts to treat prolonged episodes of FS in emergency departments or hospitals [67–69]. In 2012, Duncan et al. systematically examined mortality rates among people with FS for the first time, comparing "premature" mortality (death prior to the age of 75) among 260 people diagnosed with FS in Scotland, to the rate of premature mortality in the general Scottish population [65]. They found a significantly elevated rate of premature mortality of 0.58% annually, compared to 0.41% annually in the general population [65]. Jennum et al. identified a cohort of all 1057 people receiving a first diagnosis of FS from 2011-2016 in the Danish National Patient Registry and compared them to 2113 controls matched by age, gender, and geography [4]. They conducted a Cox proportional hazard ratio estimate and found a mortality hazard ratio of 3.21 (95% confidence interval 1.92–5.34) for people with FS [4]. In 2020 Nightscales et al. conducted a study of 674 Australian patients diagnosed with FS through video-EEG monitoring, 3064 patients diagnosed with epilepsy alone, and 175 patients diagnosed with both conditions [66]. They calculated standardized mortality ratios for each cohort by comparing mortality rates to age-, sex-, and year-specific mortality rates for the general Australian population. Overall, mortality was 2.5 times greater in the FS group than in the general population (95% confidence interval 2.0–3.3), which was not significantly different from the elevated mortality seen in the epilepsy group (standardized mortality ratio 3.3) or in the comorbid FS + epilepsy group (standardized mortality ratio 3.7). Mortality rates were especially elevated in young adults (aged 18–29) with FS, with mortality 8.6 times greater than in the young

adult general population [57]. Patients with a history of substance use disorder also had a 2.5-fold increased risk of death compared to those without. Additional psychiatric comorbidities other than substance use disorders did not further elevate the risk of mortality among people with FS [66].

The elevated mortality rate seen in Nightscales' Australian cohort [66] closely matched the elevated rate seen in Jennum's Dutch cohort [4], and Nightscales et al. expanded their analysis by reviewing causes of mortality listed by the Australian Institute of Health and Welfare. The leading causes of death among their people with FS included "epilepsy" (24%), malignancy (18%), cardiovascular disease (16%), accidental poisoning (9%), respiratory disease (7%), and suicide (7%). The fact that "epilepsy" was identified as a leading cause of death among people with FS does raise the possibility of undiagnosed comorbid epilepsy among some of the patients diagnosed with FS, although no evidence of comorbid epilepsy was found on re-review of the records of those patients who died of "epilepsy." Other possible explanations of these deaths might include epileptic seizures provoked by drugs or alcohol, or iatrogenic death caused by efforts to control prolonged episodes of functional seizures. Even excluding all deaths attributed to "epilepsy," the patients diagnosed with FS still experienced mortality more than twice that of the general population [66].

In summary, multiple studies conducted across different nations and continents have consistently demonstrated elevated mortality rates among people with FS, comparable to the elevated rates of mortality among those with epilepsy. Risk of mortality may be particularly increased relative to the general population among younger individuals, and among those with a history of substance use disorder. Common causes of death include medical illnesses such as malignancy, cardiovascular and respiratory illness, as well as self-injurious behaviors such as suicide. The growing evidence of increased mortality among people with FS should motivate neurologists and psychiatrists to prioritize evidence-based diagnosis and treatment for FS.

8. Conclusion

Functional seizures incur significant negative consequences upon patients, including psychiatric comorbidities, social consequences, financial costs, impaired QOL, and increased risk of mortality. These negative impacts are comparable in their magnitude to those affecting people with epilepsy. The clinical and scientific communities should take steps to address these negative consequences through clinical care and research that prioritizes, facilitates, and expedites evidence-based diagnosis and treatment for FS. It is also important for the scientific community to investigate the timing of these consequences and associations and their temporal relationships with the onset of FS and the diagnosis of FS in future studies.

Contributions

All authors: Study design, data collection, manuscript preparation.

Disclosures

Data availability

Not applicable.

Ethical statement

Not applicable.

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References

[1] Asadi-Pooya AA, Brigo F, Mildon B, Nicholson TR. Terminology for psychogenic nonepileptic seizures: making the case for "functional seizures". Epilepsy Behav 2020;104:106895.

[2] Brigo F, Igwe SC, Ausserer H, Nardone R, Tezzon F, Bongiovanni LG, et al. Terminology of psychogenic nonepileptic seizures. Epilepsia 2015;56:e21–5.

[3] Asadi-Pooya AA. Incidence and prevalence of psychogenic nonepileptic seizures (functional seizures): a systematic review and an analytical study. Int J Neurosci 2021:1–6.

[4] Jennum P, Ibsen R, Kjellberg J. Welfare consequences for people diagnosed with nonepileptic seizures: A matched nationwide study in Denmark. Epilepsy Behav 2019;98:59–65.

[5] Lanzillotti AI, Sarudiansky M, Lombardi NR, Korman GP, Alessio DL. Updated review on the diagnosis and primary management of psychogenic nonepileptic seizure disorders. Neuropsychiatr Dis Treat 2021;17:1825–38.

[6] Popkirov S, Asadi-Pooya AA, Duncan R, Gigineishvili D, Hingray C, Kanner AM, et al. The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities. Epileptic Disord 2019;21:529–47.

[7] Reuber M. Psychogenic non-epileptic seizures: answers and questions. Epilepsy Behav 2008;12:622–35.

[8] Hopp JL, Anderson KE, Krumholz A, Gruber-Baldini AL, Shulman LM. Psychogenic seizures and psychogenic movement disorders: are they the same patients? Epilepsy Behav 2012;25:666–9.

[9] Ekanayake V, Kranick S, LaFaver K, Naz A, Frank Webb A, LaFrance WC, et al. Personality traits in psychogenic nonepileptic seizures (PNES) and psychogenic movement disorder (PMD): Neuroticism and perfectionism. J Psychosom Res 2017;97:23–9.

[10] Walsh S, Levita L, Reuber M. Comorbid depression and associated factors in PNES versus epilepsy: systematic review and meta-analysis. Seizure 2018;60:44–56.

[11] Bermeo-Ovalle A, Kanner AM. Comorbidities in psychogenic nonepileptic seizures. In: Gates and Rowan's nonepileptic seizures. Cambridge University Press, 2018: 245-256.

[12] Diprose W, Sundram F, Menkes DB. Psychiatric comorbidity in psychogenic nonepileptic seizures compared with epilepsy. Epilepsy Behav 2016;56:123–30.

[13] Wagner MT, Wymer JH, Topping KB, Pritchard PB. Use of the Personality Assessment Inventory as an efficacious and cost-effective diagnostic tool for nonepileptic seizures. Epilepsy Behav 2005;7:301–4.

[14] LaFrance Jr. WC, Alosco ML, Davis JD, Tremont G, Ryan CE, Keitner GI, et al. Impact of family functioning on quality of life in patients with psychogenic nonepileptic seizures versus epilepsy. Epilepsia 2011; 52: 292–300.

[15] Rawlings GH, Brown I, Reuber M. Predictors of health-related quality of life in patients with epilepsy and psychogenic nonepileptic seizures. Epilepsy Behav 2017;68:153–8.

[16] Szaflarski JP, Szaflarski M. Seizure disorders, depression, and health-related quality of life. Epilepsy Behav 2004;5:50–7.

[17] Kanner AM, Schachter SC, Barry JJ, Hersdorffer DC, Mula M, Trimble M, et al. Depression and epilepsy, pain and psychogenic non-epileptic seizures: clinical and therapeutic perspectives. Epilepsy Behav 2012;24:169–81.

[18] Green B, Norman P, Reuber M. Attachment style, relationship quality, and psychological distress in patients with psychogenic non-epileptic seizures versus epilepsy. Epilepsy Behav 2017;66:120–6.

[19] Indranada AM, Mullen SA, Duncan R, Berlowitz DJ, Kanaan RAA. The association of panic and hyperventilation with psychogenic non-epileptic seizures: a systematic review and meta-analysis. Seizure 2018;59:108–15.

[20] Goldstein LH, Mellers JD. Ictal symptoms of anxiety, avoidance behaviour, and dissociation in patients with dissociative seizures. J Neurol Neurosurg Psychiatry 2006;77:616–21.

[21] Sundararajan T, Tesar GE, Jimenez XF. Biomarkers in the diagnosis and study of psychogenic nonepileptic seizures: a systematic review. Seizure 2016;35:11–22.

[22] Abubakr A, Ifeayni I, Wambacq I. The efficacy of routine hyperventilation for seizure activation during prolonged video-electroencephalography monitoring. J Clin Neurosci 2010;17:1503–5.

[23] Myers L, Trobliger R, Bortnik K, Zeng R, Saal E, Lancman M. Psychological trauma, somatization, dissociation, and psychiatric comorbidities in patients with psychogenic nonepileptic seizures compared with those in patients with intractable partial epilepsy. Epilepsy Behav 2019;92:108–13.

[24] Fiszman A, Alves-Leon SV, Nunes RG, D'Andrea I, Figueira I. Traumatic events and posttraumatic stress disorder in patients with psychogenic nonepileptic seizures: a critical review. Epilepsy Behav 2004;5:818–25.

[25] Salinsky M, Rutecki P, Parko K, Goy E, Storzbach D, O'Neil M, et al. Psychiatric comorbidity and traumatic brain injury attribution in patients with psychogenic nonepileptic or epileptic seizures: a multicenter study of US veterans. Epilepsia 2018;59:1945–53.

[26] Baslet G, Roiko A, Prensky E. Heterogeneity in psychogenic nonepileptic seizures: understanding the role of psychiatric and neurological factors. Epilepsy Behav 2010;17:236–41.

[27] Hingray C, Donne C, Cohn A, Maillard L, Schwan R, Montel S, et al. Link between psychogenic nonepileptic seizures and complex PTSD: a pilot study. Eur J Trauma Dissociation 2017;1:131–6.

[28] Boesten N, Myers L, Wijnen B. Quality of life and psychological dysfunction in traumatized and nontraumatized patients with psychogenic nonepileptic seizures (PNES). Epilepsy Behav 2019;92:341–4.

[29] Ettinger AB, Devinsky O, Weisbrot DM, Ramakrishna RK, Goyal A. A comprehensive profile of clinical, psychiatric, and psychosocial characteristics of patients with psychogenic nonepileptic seizures. Epilepsia 1999;40:1292–8.

[30] Asadi-Pooya AA, Alsaadi T, Gigineishvili D, Hingray C, Hosny H, Karakis I, et al. Social aspects of life in patients with functional (psychogenic nonepileptic) seizures: An international study. Epilepsy Behav 2020;113:107534.

[31] O'Sullivan SS, Spillane JE, McMahon EM, Sweeney BJ, Galvin RJ, McNamara B, et al. Clinical characteristics and outcome of patients diagnosed with psychogenic nonepileptic seizures: a 5-year review. Epilepsy Behav 2007;11:77–84.

[32] Duncan R, Graham CD, Oto M. Outcome at 5–10 years in psychogenic nonepileptic seizures: what patients report vs. what family doctors report. Epilepsy Behav 2014;37:71–4.

[33] Pretorius C, Cronje G. People with psychogenic non-epileptic seizures: A South African perspective. Afr J Disabil 2015;4:176.

[34] Asadi-Pooya AA, Homayoun M. Driving in patients with psychogenic nonepileptic seizures. Epilepsy Behav 2020;105:106991.

[35] Vaidya-Mathur U, Myers L, Laban-Grant O, Lancman M, Lancman M, Jones J. Socialization characteristics in patients with psychogenic nonepileptic seizures (PNES). Epilepsy Behav 2016;56:59–65.

[36] Rawat VS, Dhiman V, Sinha S, Vijay Sagar KJ, Thippeswamy H, Chaturvedi SK, et al. Co-morbidities and outcome of childhood psychogenic non-epileptic seizures–an observational study. Seizure 2015;25:95–8.

[37] Doss J, Caplan R, Siddarth P, Bursch B, Falcone T, Forgey M, et al. Risk factors for learning problems in youth with psychogenic non-epileptic seizures. Epilepsy Behav 2017;70:135–9.

[38] Asadi-Pooya AA, Bahrami Z. Education in patients with psychogenic nonepileptic seizures. Seizure 2019;64:74–6.

[39] Asadi-Pooya AA, Brigo F, Kozlowska K, Perez DL, Pretorius C, Sawchuk T, et al. Social aspects of life in patients with functional seizures: Closing the gap in the biopsychosocial formulation. Epilepsy Behav 2021;117:107903.

[40] Asadi-Pooya AA, Mesraoua B, Hingray C, Gigineishvili D, Karakis I, Hosny H, et al. Marital status in patients with functional (psychogenic nonepileptic) seizures: An international study. Epilepsy Behav 2020;112:107461.

[41] Johnstone B, Malpas CB, Velakoulis D, Kwan P, O'Brien TJ. Psychiatric symptoms are the strongest predictors of quality of life in patients with drug-resistant epilepsy or psychogenic nonepileptic seizures. Epilepsy Behav 2021;117:107861.

[42] Avalos JC, Silva BA, Tevés Echazu MF, Rosso B, Besocke AG, del Carmen Garcia M. Quality of life in patients with epilepsy or psychogenic nonepileptic seizures and the contribution of psychiatric comorbidities. Epilepsy Behav 2020;112:107447.

[43] Karakis I, Montouris GD, Piperidou C, Luciano MS, Meador KJ, Cole AJ. Patient and caregiver quality of life in psychogenic non-epileptic seizures compared to epileptic seizures. Seizure 2014;23:47–54.

[44] Asadi-Pooya AA, Farazdaghi M. Driving rate in patients with seizures: epilepsy vs functional seizures. Epilepsy Behav 2021;119:107985.

[45] Ye K, Foster E, Johnstone B, Carney P, Velakoulis D, O'Brien TJ, et al. Factors associated with subjective cognitive function in epilepsy and psychogenic non-epileptic seizures. Epilepsy Res 2020;163:106342.

[46] Karaaslan Özgül, Hamamcı M. Cognitive impairment profile differences in patients with psychogenic non-epileptic seizures and epilepsy patients with generalized seizures. Neurol Res 2020;42:179–88.

[47] Kausar N, Qurban H, Bibi B. A comparative study to investigate the level of cognitive impairment among epileptic and psychogenic non-epileptic patients. J Pak Med Assoc 2021;71:420–3.

[48] Cáceres C, Grau-López L, Martínez S, Mariscal C, González-Fuxà A, Jiménez M, et al. Psychogenic nonepileptic seizures: The effect of accurate diagnosis on cognition. Epilepsy Behav 2021;117:107766.

[49] Simani L, Roozbeh M, Rostami M, Pakdaman H, Ramezani M, Asadollahi M. Attention and inhibitory control deficits in patients with genetic generalized epilepsy and psychogenic nonepileptic seizure. Epilepsy Behav 2020;102:106672.

[50] Rosales R, Dworetzky B, Baslet G. Cognitive-emotion processing in psychogenic nonepileptic seizures. Epilepsy Behav 2020;102:106639.

[51] Asadi-Pooya AA, Bahrami Z. Risk factors for the use of antiepileptic drugs in patients with psychogenic nonepileptic seizures. Epilepsy Behav 2019;90:119–21.

[52] Ahmedani BK, Osborne J, Nerenz DR, Haque S, Pietrantoni L, Mahone D, et al. Diagnosis, costs, and utilization for psychogenic non-epileptic seizures in a US health care setting. Psychosomatics 2013;54:28–34.

[53] Magee JA, Burke T, Delanty N, Pender N, Fortune GM. The economic cost of nonepileptic attack disorder in Ireland. Epilepsy Behav 2014;33:45–8.

[54] Martin RC, Gilliam FG, Kilgore M, Faught E, Kuzniecky R. Improved health care resource utilization following video-EEG-confirmed diagnosis of nonepileptic psychogenic seizures. Seizure 1998;7:385–90.

[55] Seneviratne U, Low ZM, Low ZX, Hehir A, Paramaswaran S, Foong M, et al. Medical health care utilization cost of patients presenting with psychogenic nonepileptic seizures. Epilepsia 2019;60:349–57.

[56] Nunez-Wallace KR, Murphey DK, Proto D, Collins RL, Franks R, Chachere DM, et al. Health resource utilization among US veterans with psychogenic nonepileptic seizures: A comparison before and after video-EEG monitoring. Epilepsy Res 2015;114:114–21.

[57] Russell LA, Abbass AA, Allder SJ, Kisely S, Pohlmann-Eden B, Town JM. A pilot study of reduction in healthcare costs following the application of intensive short-term dynamic psychotherapy for psychogenic nonepileptic seizures. Epilepsy Behav 2016;63:17–9.

[58] Jones B, Reuber M, Norman P. Correlates of health-related quality of life in adults with psychogenic nonepileptic seizures: A systematic review. Epilepsia 2016;57:171–81.

[59] Myers L, Lancman M, Laban-Grant O, Matzner B, Lancman M. Psychogenic non-epileptic seizures: predisposing factors to diminished quality of life. Epilepsy Behav 2012;25:358–62.

[60] Strutt AM, Hill SW, Scott BM, Uber-Zak L, Fogel TG. Motivation, psychopathology, locus of control, and quality of life in women with epileptic and nonepileptic seizures. Epilepsy Behav 2011;22:279–84.

[61] Scévola L, Wolfzun C, Sarudiansky M, Pico MMA, Ponieman M, Stivala EG, et al. Psychiatric disorders, depression and quality of life in patients with psychogenic non-epileptic seizures and drug resistant epilepsy living in Argentina. Seizure 2021;92:174–81.

[62] Salinsky M, Rutecki P, Parko K, Goy E, Storzbach D, Markwardt S, et al. Health-related quality of life in Veterans with epileptic and psychogenic nonepileptic seizures. Epilepsy Behav 2019;94:72–7.

[63] Gagny M, Grenevald L, El-Hage W, Chrusciel J, Sanchez S, Schwan R, et al. Explanatory factors of quality of life in psychogenic non-epileptic seizure. Seizure 2021;84:6–13.

[64] Goldstein LH, Robinson EJ, Mellers JDC, Stone J, Carson A, Reuber M, et al. CODES study group. Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial. Lancet Psychiatry 2020;7:491–505.

[65] Duncan R, Oto M, Wainman-Lefley J. Mortality in a cohort of patients with psychogenic non-epileptic seizures. J Neurol Neurosurg Psychiatry 2012;83:761–2.

[66] Nightscales R, McCartney L, Auvrez C, Tao G, Barnard S, Malpas CB, et al. Mortality in patients with psychogenic nonepileptic seizures. Neurology 2020;95:e643–52.

[67] Howell S, Owen K, Chadwick D. Pseudostatus epilepticus. QJM: Int J Med 1989;71:507–19.

[68] Reuber M, Baker GA, Gill R, Smith DF, Chadwick DW. Failure to recognize psychogenic nonepileptic seizures may cause death. Neurology 2004;62:834–5.

[69] Dworetzky BA, Bubrick EJ, Szaflarski JP. Nonepileptic psychogenic status: markedly prolonged psychogenic nonepileptic seizures. Epilepsy Behav 2010;19:65–8.