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Psychogenic nonepileptic seizures in adults with epilepsy and intellectual disability: A neglected area

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ABSTRACT

Purpose: To describe the main characteristics of psychogenic nonepileptic seizures (PNES) in adults with epilepsy and intellectual disability (ID), and to analyse the differences regarding psychosocial functioning, epilepsy severity and ID between patients with PNES and a control group without PNES.
Methods: Medical records of adults with ID and epilepsy living at an epilepsy care facility (N = 240) were screened for PNES and evaluated by a neurologist. A control group consisting of patients with epilepsy and ID, without PNES, was matched according to age, sex and level of ID. Characteristics of PNES and epilepsy were provided by the subject's nursing staff or retrieved from patient charts, psychosocial data were collected by standardised questionnaires and level of ID was individually assessed using psychometric instruments.
Results: The point prevalence of PNES was 7.1%. The patients with PNES (n = 15) were most often female and had a mild or moderate level of ID. Compared to controls, they showed more depressive symptoms, experienced more negative life events and had more often an ID discrepancy (ID profile with one domain particularly more impaired than another). Stress-related triggers were recognised in a large majority by the nursing staff.
Conclusion: PNES appears to be a relatively rare diagnostic entity among inpatients with both epilepsy and ID. However, the complexity of diagnosing PNES in this population, and the similarities in stress-related triggers for PNES in patients with and without ID, suggest that PNES may be underdiagnosed in the ID population. Diagnostic challenges of PNES and, as subcategory, reinforced behavioural patterns are discussed.

1. Introduction

Psychogenic non-epileptic seizures (PNES) are defined as sudden and involuntary paroxysmal events that resemble epileptic seizures, but are not induced by an organic cause. In addition, there is positive evidence or it is strongly suspected that the events are related to a psychogenic cause. These events can involve changes in behaviour, motor activity, sensation, cognitive processing, or autonomic function [1,2]. The term PNES can be misleading, as one not only needs to exclude epilepsy, but also other organic causes that can lead to a similar semiology.

The diagnosis of PNES consists of a two-phase process, of which the patient needs to be informed as soon as possible. First, organic causes, including especially epilepsy, have to be excluded as a cause of the seizures. Epilepsy may coincide with PNES, however, and it is necessary to determine whether or not the paroxysmal event can be attributed to epilepsy. The gold standard for excluding epilepsy is video-EEG monitoring of a characteristic seizure that does not show the electrographic discharges seen during an epileptic seizure [2,3]. In the second phase, psychological aetiologies that cause the paroxysmal events must be assessed.

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The highest level of certainty, "documented PNES", is reached when a non-epileptic seizure with semiology typical to PNES is captured on video-EEG, along with a patient history of psychosocial characteristics consistent with PNES [2]. As this certainty level cannot always be reached, for example because of limited access to video EEG, the recognition of PNES with a lower level of certainty (i.e., "possible", "probable", or "clinically established") also becomes relevant.

PNES is considered to be a multifactorial biopsychosocial disorder [4]; many psychosocial and biological factors have been described that contribute to its development or prolongation (e.g., [1,5]. Studies have shown that the majority of patients with PNES are female (75%) and report previous trauma (up to 70%); also, a history of co-morbid psychiatric or psychosocial problems is common [2].

PNES are also recognised among patients with ID (e.g., [6,7,4]. A below average intelligence quotient (i.e. IQ <85) might be a risk factor for PNES [8], although it remains unclear whether this study also included patients with ID (IQ <70). There is limited evidence regarding the presentation and incidence of PNES in this subpopulation, as patients with ID are often excluded from studies. Duncan and Oto [9] compared patients with PNES with and without ID and concluded that a diagnosis of epilepsy, the use of anti-epileptic drugs, episodes of psychogenic nonepileptic status, and situational or emotional triggers were more prevalent among those with ID. Sexual abuse seemed to be more frequent among those without ID. Another theory suggested that PNES in people with ID manifests less profoundly as an emotional conflict, but more as a reinforced behavioural pattern, which can be considered a subcategory of PNES. By exhibiting this reinforced behavioural pattern a secondary gain is reached, such as receiving attention or avoiding demands or unpleasant situations [10]. By producing seizure-like events that are paradoxically reinforced by caregivers, these patients may have unconsciously and unintentionally learned how to control the environment. This idea was elaborated upon in a study by Magudda et al. [11], who described characteristics of a patient group with mild ID. Remarkably, this subgroup developed PNES after a decrease in epileptic seizure frequency. All of these patients had early-onset epilepsy, for which caregivers probably provided much attention. The authors hypothesise that the decrease in epileptic seizure frequency or cessation of epilepsy might have led to a loss of this advantage, after which the epileptic seizures had been substituted by PNE Baslet et al. [6] identified a subgroup of PNES patients who presented with neurological impairments and ID, but showed less severe psychiatric impairment. Psychopathology, including depression, anxiety and somatic distress, was often present, however.

The aims of the present study are twofold: (1) to describe (clinical) characteristics of PNES in adults with ID and epilepsy, and (2) to compare epilepsy severity and psychological and behavioural characteristics between those with PNES and a matched control group without PNES, all with epilepsy and ID.

2. Methods

2.1. Participants

Electronic charts of adult patients living at the residential care facility of Kempenhaeghe, a tertiary epilepsy centre in The Netherlands, were screened for evidence of non-epileptic events between January 2014 and December 2016. Only those who met the following criteria were included: impaired intellectual functioning (IQ < 70), age $\geq$18 years, and diagnosis of PNES following evaluation by a neurologist and, when necessary, other medical specialists. Those with PNES must have had more than one seizure-like event in the past two years, which had to include a hypothesised behavioural or psychosocial component. Seizures with an organic cause were excluded. In this article we consider the reinforced behavioural pattern as a subcategory of PNES. Our screening of 240 eligible patients yielded 17 patients with PNES (7.1%). As two patients did not provide consent for the study, a total of 15 subjects with PNES were included in the final analyses.

A control group consisting of 15 patients with epilepsy and ID, without PNES, was matched according to age, sex, and level of ID. For each PNES subject, all matching patients were identified and one of the possible matched was randomly automated selected.

2.2. Instruments and procedure

This cross-sectional, observational study is part of the TRIANGLE study (The Relation between epilepsy, ID, And Neuropsychiatric comorbidities in a Group of patients in Long-term care for Epilepsy). TRIANGLE is approved by the local ethical committee of Kempenhaeghe (No. 15.01). All subjects or legal representatives (if appropriate) provided consent for the study.

All information regarding PNES was collected through a questionnaire completed by the subject's nursing staff (see Appendix A). This questionnaire was created by a research team including a health care psychologist, psychotherapist and neurologist. Both objective (e.g., frequency, time and location, and injuries as a result of PNES) as well as subjective characteristics (e.g., suspected triggers and impact on daily life) were addressed.

The level of ID was diagnosed according to DSM-5 in terms of mild, moderate, severe or profound [12]. Each ID domain, i.e., conceptual, social and practical, was assessed separately using an abbreviated version of the Wechsler Adult Intelligence Scale – fourth edition [26] and the Vineland-II subscales Socialization and Daily Living Skills [14]. A significant difference between domains was considered to be an ID domain discrepancy (for more information regarding this method, see [13]).

The severity of epilepsy was determined using the Epilepsy Impact Scale Kempenhaeghe (EPIEK; [15], which is based on five aspects: seizure frequency, number of anti-epileptic drugs, use of emergency anti-epileptic drugs, use of protective measures for epilepsy, and adjustments in the subject's daily schedule after a seizure. The relevant information was retrieved from the subject's medical records. The EPIEK yields an epilepsy severity score ranging from 0 to 10, a higher score indicating a more severe form of epilepsy.

For the assessment of depressive symptoms, anxiety symptoms, aggressive/destructive behaviour, and life events, three standardised questionnaires were administered among the subject's nursing staff. Depressive and anxiety symptoms were assessed using the Anxiety, Depression, And Mood Scale (ADAMS) [16,17] and aggressive/destructive behaviour was assessed using the Behavior Problems Inventory (BPI) [18,19], higher scores reflecting more severe symptoms or behaviour. Both the ADAMS and BPI have been validated among people with ID [17,18]. The number of life events in the past year was calculated using the Checklist Life Events (CLE) [20,21].

2.3. Analyses

First, clinical characteristics of PNES are described. The correlation between frequency of PNES and epileptic seizures in the past year was examined using Spearman's rank correlation analysis. As neither variable met the criteria for a normal distribution, a log-transformation was performed prior to the analysis. Second, differences between subjects with PNES and the control group are analysed with statistical analyses appropriate for case-control studies, i.e., paired T-test or Wilcoxon signed rank test

for continuous variables and McNemar's test for dichotomous variables. All analyses were conducted two-tailed, with *p*-values <.05 considered statistically significant.

3. Results

The age of PNES subjects ranged from 19.3 to 70.6 years (mean = 46.6 years, SD = 15.6) and did not differ from the controls (mean = 45.9, SD = 15.2, $p = .588$). The majority were of female gender (66.7%) and had a mild or moderate level of ID (33.3% and 40.0%, respectively). All subjects had had at least one seizure in the past year and were prescribed daily anti-epileptic drugs.

3.1. PNES characteristics

The PNES diagnosis was based on video-EEG in 53.3%, on video evaluation by a neurologist in 13.3%, and on history-taking in the remaining cases. In 80% of subjects, the semiology of PNES showed similarities with an epileptic seizure type which the subject also regularly presented. Most common were tonic-like, tonic-clonic-like and absence-like seizures. PNES started during adulthood in two-thirds of cases; in the majority (80.0%), PNES occurred at various times of day and at various locations. There were, however, subjects who showed PNES only in the morning (n = 1), only at night (n = 1), or only in the evening (n = 1). In only three cases did the PNES occur at the subject's residence. The frequency of PNES was mostly weekly (40.0%) or monthly (40.0%); the remaining three subjects exhibited PNES (almost) daily. Patient files showed that epileptic seizures were recorded more frequently than PNES in 73.3% cases. There was a tendency towards a negative association between the frequency of PNES and epileptic seizures (Spearman's $r = -.453$, $p = .090$).

A psychiatrist was involved in the clinical care of over half the subjects (53.3%); 26.7% had an comorbid psychiatric diagnosis. Also, daily use of psychotropic medication for treatment of psychiatric, psychological or behavioural problems was common (53.3%). According to the nursing staff, triggers for PNES were identified in the majority (86.7%). These triggers involved stress, negative mood, unexpected events, (over)demanding situations and overstimulation. The nursing staff responded to PNES by ignoring the seizure or distracting the patient in 53.3%. In other cases they soothed the patient, tried to start a conversation or responded as they would to an epileptic seizure. Small injuries as a result of PNES were reported in 26.7%; the PNES had an impact on daily life in 60.0% of subjects. Clinical characteristics of the PNES group are described in Appendix B.

3.2. PNES subjects versus controls

Associations with respect to epilepsy severity and psychological characteristics between the PNES and control group are presented in Table 1. Of the continuous variables, the number of negative life events and the severity of aggressive/destructive behaviour did not meet the normality assumption. Therefore, Wilcoxon signed rank tests were performed as non-parametric alternative of paired T-tests.

Both the PNES and control group had had at least one epileptic seizures in the past year and were using anti-epileptic drugs on a daily basis. The epilepsy in both groups was severe, with a median severity score of nearly 7 in the PNES group and 6 in the control group using a scale from 0 to 10 (not statistically significant). The PNES group differed from the control group with respect to psychological characteristics. Paired T-tests indicated that PNES subjects had significantly more depressive symptoms than controls (mean difference = 6.3, $t(14) = 2.39$, $p = .031$). Although they also had a higher mean score on anxiety symptoms and a higher median score on aggressive behaviour, these differences were too small to reach statistical significance ($p = .212$ and $p = .529$, respectively). Furthermore, PNES subjects had experienced significantly more negative life events in the past year ($Z = -2.61$, $p = .009$), such as major injuries, decline in mobility and severe illness or death of a friend or family member. The history of critical life events at an earlier age was unknown for most subjects, as well as possible traumas. There was a trend indicating that a psychiatrist was more frequently involved in the care of PNES subjects compared to the control group ($p = .070$). PNES subjects also had an ID domain discrepancy ($p = .013$) more often than controls, which was usually at the expense of social or practical adaptive skills (50% and 40%, respectively). A higher percentage of PNES subjects used psychotropic drugs (53.3% versus 26.7%) and had a comorbid psychiatric diagnosis (26.7% versus 13.3%; e.g., autism spectrum disorder, depression), although these differences did not reach statistical significance ($p = .289$ and $p = .625$, respectively).

4. Discussion

In this study on PNES in patients with epilepsy and ID, we found that two-thirds of our PNES sample was female, which is in line with the general findings on PNES in people without ID [2]. The semiology of PNES was heterogeneous and included mostly tonic-clonic-like, tonic-like, or absence-like seizures. Often, the semiology showed similarities with one of the epileptic seizure types of the patient. As this research took place in a tertiary epilepsy centre,

Table 1
Differences between PNES and control group.

Characteristics	PNES		Control group		*P* value
Epilepsy severity	*M* = 6.93	SD = 1.33	*M* = 5.80	SD = 3.00	n.s.[a]
Depressive symptoms	*M* = 12.87	SD = 8.33	*M* = 6.53	SD = 4.60	<.05[a]
Anxiety symptoms	*M* = 5.53	SD = 4.41	*M* = 3.87	SD = 2.97	n.s.[a]
Negative life events	*Mdn* = 4	IQR = 2–7	*Mdn* = 2	IQR = 1–2	<.01[b]
Aggressive behaviour	*Mdn* = 2	IQR = 0–7	*Mdn* = 1	IQR = 1–4	n.s.[b]
Daily use psychotropic drugs	53.33%		26.67%		n.s.[c]
Comorbid psychiatric diagnosis	26.67%		13.33%		n.s.[c]
Psychiatrist involved	53.33%		13.33%		<.10[c]
ID domain discrepancy[d]	66.67%		13.33%		<.05[c]

[a] Paired T-test.
[b] Wilcoxon signed rank test.
[c] McNemar's Test.
[d] A discrepancy indicated a significant intra-individual difference between two out of three domains of adaptive functioning (conceptual, social, or practical domain).
PNES = (Psychogenic) nonepileptic seizures; ID = Intellectual disability; M = Mean; SD = Standard deviation; Mdn = Median; IQR = Interquartile range; n.s. = not significant.

all subjects had active epilepsy (all had had at least one seizure in the past year).

In line with the literature on PNES in people without ID, the patients in our sample showed psychosocial vulnerabilities as well. The triggers for PNES that were identified by the nursing staff (in 87% of cases) included mostly stress-related situations, such as unexpected events, (over)demanding situations, and overstimulation. Another risk factor was a depressive mood. The relevance of psychosocial aspects, possibly in the development of PNES, is confirmed by the findings of our case-control study: patients with PNES had higher levels of depressive symptoms and had experienced more negative life events (medians 4 versus 2), which could relate to trauma (recollections). Patients with PNES also had significantly more often an ID domain discrepancy (67% versus 13%), in which the person had relatively poorer skills on one domain of adaptive functioning compared to another domain. This indicates that professionals should be aware of the risk of overestimating the person in order to avoid (over)demanding situations. Furthermore, the PNES group also had higher rates of comorbid psychiatric diagnoses, involvement of a psychiatrist in their clinical care (because of psychological or behavioural problems), and daily use of psychotropic medication than the control group, although statistical significance was not reached.

There seemed to be a tendency towards a negative association between the frequency of PNES and epilepsy, although only inter-individually. This might be in accordance with results from Magudda et al. [11], who described that patients with a mild ID developed PNES after a decrease in epileptic seizure frequency. They suggest that this decrease might have led to a reduction in attention received from caregivers, and in order to compensate for this loss of advantage, patients subconsciously learned to display PNES instead. When the epilepsy severity between those with and without PNES was compared, the difference was not statistically significant in our study. There were some patients who only showed PNES at a particular location or time of day, which might indicate that there was a situational trigger. Such situational triggers were found to be more prevalent among patients with ID in previous research [9]. PNES in this patient group may be characterised by a behavioural pattern that is reinforced by the environment in some patients, especially in those with a situational trigger or low epileptic seizure frequency. This reinforced behavioural pattern should not be confused with intentional simulation, however. To further investigate this theory, more extensive longitudinal research is necessary, including clinical observations of antecedents and consequences of PNES and an assessment of coping style. Although the subjects came from one tertiary care facility, which increases homogeneity and reliability of data sampling, they constituted a small sample size and hence poor statistical power.

In our study sample, the PNES diagnosis was confirmed by video-EEG in about half of the patients and by video evaluation by a neurologist in 13%, which means that a substantial number of subjects had an “unconfirmed” diagnosis of PNES. The level of certainty of PNES according to LaFrance et al. [2] was difficult to assess in this sample. In some cases, the non-epileptic event was captured on video EEG, but the history of psychosocial factors consistent with PNES was questionable, for example because valid and reliable instruments to assess psychological aspects in people with ID are limited and people with ID themselves are less capable of reliably noticing or explaining psychosocial aspects. In other cases, the PNES semiology was positively evaluated by a neurologist and psychosocial triggers were identified, but a video EEG assessment was not considered feasible by the multidisciplinary team, because of the relatively low frequency of PNES and potential burden for the – often vulnerable – patient. As all of our subjects also had active epilepsy, results on (video-)EEG showed epileptiform activity in most cases which complicated the differential diagnosis. Although clinical decisions on the care for people with ID should always take into account the potential burden for the patient, a comprehensive assessment of suspected PNES is important to prevent over- or undertreatment, especially given the reported impact on daily life in the majority of patients in our study.

The point prevalence of 7.1% we found is clearly below reported diagnostic rates of PNES in the general population, varying from 12% to 30% for patients referred to a tertiary epilepsy centre [25,22]. Nor does it match the evidence from Reuber et al. [8], suggesting that an IQ below average is a risk factor for PNES. Perhaps this risk factor does not apply to our patient population who predominantly had a more severe level of ID. Other explanations rather than a very low IQ for the low prevalence might be the diagnostic challenges with respect to non-epileptic events, the retrospective nature of this study, or difficulties in the differentiation between PNES and epilepsy in individuals with ID, which have been observed in previous studies [23,24]. As a more severe level of ID is associated with a more severe epilepsy [13], PNES may have been overshadowed by epilepsy. To address these issues, future research should use a prospective study design and include outpatients with ID. Considering the very low number of subjects and incomplete diagnostic processes in our study, the significant differences between patients with and without PNES are remarkable and emphasize that our PNES sample is a distinct subgroup.

5. Conclusion

This clinical study describes the main characteristics of PNES among inpatients with ID and epilepsy, a neglected and vulnerable subpopulation. An important diagnostic challenge includes the difficult differentiation between PNES and somatic or behavioural comorbidities, overshadowing by severe epilepsy (and therefore PNES may not be recognised or misinterpreted by caregivers), and the limited tools available to assess psychogenic factors as psychological aetiologies for non-epileptic seizures that are appropriate for people with ID. This emphasizes the importance of a multidisciplinary approach, involving health professionals who are experienced in working with people with epilepsy and ID. Professionals should be aware of the possibility of PNES in people with ID and the similarities with the adult PNES population without ID, including a female predisposition, psychological or psychiatric comorbidities and (traumatic) life events. Cases with PNES usually had a mild or moderate ID and an ID domain discrepancy. Especially in those with a more severe level of ID and/or impaired social-emotional functioning, a reinforced behavioural pattern might also be considered as a subcategory of PNES. Enhanced diagnostics of PNES in patients with ID is important for the development of a systematic approach to detect PNES and to provide evidence-based treatment.

Declarations of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.seizure.2018.05.002.

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