



The effect of attachment style on long-term outcomes in psychogenic nonepileptic seizures: Results from a prospective study



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ABSTRACT

Introduction: Insecure and fearful attachment styles have been reported in psychogenic nonepileptic seizures (PNES). We have investigated associations between long-term clinical outcome in PNES, parenting and attachment styles and demographic, clinical, and neuropsychiatric factors.

Material and methods: Patients aged at least 16 years and with documented PNES, according to criteria from the International League Against Epilepsy, were prospectively recruited to this study. They were assessed at baseline to determine clinical characteristics, experience of attachment and perceptions of experienced parenting styles, trauma history, dissociation, and health-related quality of life. At a mean of 70.45 (SD 29.0, range 22–130) months after inclusion, participants were contacted by telephone and asked about their current medical status and psychiatric/psychological interventions.

Results: Of 53 patients included in the study, 51 (96 %) provided follow-up data. Most (84.9 %) patients were female, and the mean age of PNES onset was 25.6 years. At follow-up, 20 patients (39 %) were free of PNES. Those patients that had achieved PNES freedom at follow-up had lower levels of attachment anxiety ($p = 0.01$) and reported to have experienced their fathers as less controlling ($p = 0.02$) and their mothers as more caring ($p = 0.04$) at baseline compared with those patients still suffering from PNES. Seizure freedom at follow-up was predicted by male gender, younger age at PNES onset, and less attachment anxiety.

Conclusion: In our cohort from a tertiary epilepsy center the long-term prognosis of PNES is poor. Attachment anxiety is a risk factor for persistent PNES. It may be of therapeutic relevance to assess attachment patterns in patients with PNES.

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1. Introduction

Psychogenic nonepileptic seizures (PNES) is classified as a conversion disorder in DSM-5 [1] and as a dissociative disorder in ICD-10 [2]. Patients with PNES are commonly encountered in neurology clinics [3]. Misdiagnosis, long delays to diagnosis, and inappropriate treatment with anti-seizure medications occur commonly in patients with PNES [4,5]. PNES is associated with high rates of economic inactivity [6] and disability [7]. The prognosis in adults is probably poor: although the quality of follow-up studies is variable, approximately two-thirds of newly diagnosed adults continue to have seizures many years after receiving their diagnosis [8–13].

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Individuals with PNES have a high prevalence of traumatic life events, neglect, and family dysfunction [14]. Dysfunctional parenting has been related to personality pathology in adult life [15] and to mental disorders in adolescents [16] and adults [17]. Adults with PNES have been reported to have received less parental care than patients with other conversion disorders [18], whereas a study on children did not find a difference in perceived parenting between children with PNES and their siblings [19].

Attachment theory may provide a link between early traumatic events, family dysfunction, and psychopathological conditions. According to attachment theory, early childhood interactions with primary caregivers result in patterns of thoughts, beliefs, emotions, and behaviors regarding self and others, referred to as attachment styles [20,21]. Attachment disturbances have been associated with several mental disorders [22]. In patients with PNES, a predominance of fearful attachment [23] and insecure attachment [24]

have been reported. Attachment styles may also influence outcomes in psychotherapy generally [25]. However, in patients with PNES, this potential association has not been investigated.

We conducted a prospective cohort study to investigate clinical outcomes in adult patients with PNES and possible associations between experienced parenting and attachment styles, along with demographic, clinical, and neuropsychiatric factors. We hypothesized that insecure attachment styles, and patient perceptions of poor parental bonding may be associated with a less successful clinical outcome in patients with PNES receiving the usual care and follow-up.

2. Material and methods

2.1. Clinical setting

Patients are referred for diagnosis to the Norwegian Epilepsy Center (NEC) by neurologists, pediatricians, and general practitioners. Patients undergo a diagnostic work-up, clinical evaluation, revision of MRI of the brain, observation, video-electroencephalography (EEG), and psychological evaluation. When a diagnosis of PNES is confirmed, the diagnosis is explained to the patient and relatives by the physician. Patients and families are provided with further information on PNES by a staff nurse and are then invited to a follow-up stay of 2–4 week duration for further psychoeducation from a multidisciplinary team. This team is composed of epileptologists (neurologists and pediatricians), psychologists, nurses, a social worker, an occupational therapist, and a physical therapist. Patients are usually referred to their local psychiatry outpatient department or to the local community psychiatric health team.

2.2. Study sample

From September 2009 to October 2017, we prospectively recruited consecutive patients, aged 16 years and older, from the NEC. Due to organizational changes at the center, there were periods with no patient inclusion during 2010, 2013, and 2016. Patients were recruited to the study either at the end of a diagnostic stay, when a PNES diagnosis was confirmed, or during a follow-up stay. All patients had a documented PNES diagnosis from an experienced epileptologist at the NEC, i.e., a history indicative for PNES and witnessed events while on video-EEG, consistent with the highest degree of certainty of PNES according to criteria from the International League Against Epilepsy [26].

Some authors have claimed that PNES rather than being an entity of its own, has to be regarded as a symptom of underlying psychiatric disorders [27]. In this study, we have chosen to define PNES as a disorder following the classification systems of ICD-10 [2] and DSM-5 [1].

Three experienced neurologists at NEC (CL, MIL, AV) prospectively collected baseline demographic and medical data. The patients were interviewed and medical records were reviewed to ascertain PNES diagnosis, age at PNES onset, and EEG and MRI abnormalities, and to rule out the presence of comorbid epilepsy. Patients with comorbid epilepsy were excluded. Further inclusion and exclusion criteria are listed in Table 1.

A total of 62 patients were invited to join the study, four of whom declined. A further two did not meet our study criteria on review of the records. One patient died during the study, and as undiagnosed concomitant epilepsy was thought possible, she was also excluded. Two patients withdrew their consent during the study, leaving 53 participants for the analyses.

Table 1
Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Documented PNES diagnosis according to criteria from the International League Against Epilepsy	Estimated low (<70) IQ
Age 16 years or older	Patients with severe medical and/or psychiatric conditions expected to be unable to undergo the planned assessment

2.3. Psychometric measures

The following self-report questionnaires were used at baseline: The Attachment Style Questionnaire (ASQ), Parental Bonding Instrument (PBI), Traumatic Experience Checklist (TEC), Dissociative Experience Scale (DES), Somatoform Dissociation Questionnaire (SDQ-20), and a visual analog health thermometer (EQ-VAS). Other than EQ-VAS [28], none of the Norwegian versions of these questionnaires has been clinically validated.

2.3.1. Attachment style Questionnaire (ASQ)

The ASQ [29] is a 40-item self-reporting measure of adult attachment dimensions. Items are rated on a 6-point Likert scale (1 (totally disagree) to 6 (totally agree)). A higher score indicates a greater amount of the attachment construct measured. The following attachment dimensions were derived: “confidence in relationships” that assesses secure attachment, “discomfort with closeness” and “relationships as secondary” both of which assess aspects of attachment avoidance, and “need for approval” and “preoccupation with relationships” that are both aspects of attachment anxiety. Consistency coefficients (Cronbach’s alpha) showed good reliability for the five dimensions in the present study, ranging from 0.80 to 0.84.

2.3.2. Parental bonding instrument (PBI)

The Norwegian version [30] of PBI [31,32] was used to assess maternal and paternal parenting styles recalled from the first 16 years of each patient’s life. It consists of 25 items answered on a 4-point Likert scale (1 (very like) to 4 (very unlike)). The PBI measures two fundamental dimensions of interpersonal relationships, including parental behavior: ‘care’ and ‘protection’. Combining these two dimensions enables sorting of the patient’s parents into one of the four categories, including affectionless control (low care, high protection), affectionate constraint (high care, high protection), neglectful (low care, low protection), and optimal parenting (high care, low protection). Previous studies of PBI have shown satisfactory reliability and validity estimates [33]. In our study, the four PBI subscales showed excellent internal reliability, with Cronbach’s alpha ranging from 0.87 (subscale paternal protection) to 0.93 (subscale maternal care).

2.3.3. Traumatic experience checklist (TEC)

The TEC [34] is a 29-item self-report questionnaire assessing potentially traumatic experiences, including a wide range of experiences. It has a total score and distinguishes between five subscales: emotional neglect, emotional abuse, threat to body/life, sexual harassment, and sexual abuse. Previous studies have shown satisfactory reliability and validity [35].

2.3.4. Dissociative experience scale (DES)

The DES [36] is a 28-item self-report inventory of dissociative phenomena. It provides a total score and three subscales: depersonalization–derealization, amnesic dissociation, and

absorption and Imaginative Involvement. It is reported to be reliable, internally consistent, and temporally stable [37]. In our study, reliability for the three subscales was good with consistency coefficients (Cronbach's alpha) ranging from 0.78 to 0.84.

2.3.5. Somatoform dissociation Questionnaire (SDQ-20)

The SDQ-20 [38] measures the severity of somatoform dissociation. It includes 20 items that are to be rated on a 5-point Likert scale (1 (not at all) to 5 (extremely)). To obtain an index of symptom levels, the scores across the items are summed (total index ranges from 20 to 100). Cronbach's alpha was 0.79, indicating good reliability.

2.3.6. Visual analog health thermometer (EQ-VAS)

General health was assessed using a visual analog scale similar to a thermometer, which is part of the EuroQol (EQ-5D) instrument [39]. It assesses overall health status, ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).

2.4. Follow-up

At a mean of 71 (SD 29.0, 22–130) and a median of 66 months month after inclusion, participants were contacted by telephone and, following a structured interview guide, asked about current medical status (e.g., PNES frequency, employment status, and hospital admissions) and psychiatric/psychological interventions (e.g., psychotherapy, other nonpharmacological interventions).

Statistics based on our hypothesis suggested that insecure attachment would be associated with persistent PNES-seizures at follow-up; the power analysis suggested at least 88 participants each with insecure attachment and with secure attachment to detect a difference in proportions of PNES-free patients at follow-up of 20 % in the group with insecure attachment vs 50 % seizure-free participants at follow-up in the group with secure attachment with a maximum risk of 5 % of committing a type 1-error and a statistical power of 80 %. For the cutoff between secure and insecure attachment, we used 2 Standard Deviations (SD) below the normative mean on the confidence-scale of the ASQ (<=34.6) [40].

Baseline and follow-up characteristics were assessed for differences between patients who were seizure free at follow-up, defined as absence of PNES during the previous year, and not seizure free at follow-up. Student's t-test was used for continuous and normally distributed variables, Mann-Whitney U-test for ordinal or skewed variables, and chi-square tests or Fisher's exact tests for categorical data. In addition, we examined within-group differences according to the secondary outcomes, >=50 % seizure reduction.

All hypothesis testing was 2-tailed. To correct for multiple comparisons when assessing group differences on baseline and follow-up characteristics (>20 variables) (Table 3) we considered p values of <=0.01 as statistically significant, otherwise p values of <=0.05 were considered as statistically significant.

To determine potential predictors of achieving PNES freedom by time of follow-up, we performed multivariate logistic regression analysis. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS, version 26, IBM). Missing items were replaced with the mean of the answered items in the subscale, if at least half of that subscale had been answered.

2.5. Ethics

The present study was approved by the Regional Committee for Medical Research Ethics South East Norway (2009/1078/REC

South-east). The study was conducted and reported in accordance with the STROBE checklist.

3. Results

51 (96 %) of the original 53 participants provided data at follow-up, as two participants were lost to follow-up.

Of all 53 patients originally included, 45 (85 %) were female, the mean age at PNES onset was 25.6 years, and the mean age at presentation was 32.1 years, with a mean diagnostic delay of 5.6 years. There was a prior psychiatric history of anxiety or depression in 32 (60 %) of the 53 participants and 45 (85 %) had experienced at least one traumatic life event. For baseline characteristics see Table 2.

Regarding attachment styles, our sample of patients with PNES showed significantly lower levels of confidence (security) (p < 0.0001) and higher levels of insecurity on attachment styles than a normative sample. The mean confidence score for our patients with PNES was 32.3 (SD = 7.3) whereas the mean confi-

Table 2
Baseline characteristics of the PNES sample.

Baseline characteristics	Values (n = 53)
Female gender, n (%)	45 (84.9)
Age at presentation, y, mean (SD, range)	32.1 (13.4, 16–62)
Age at PNES onset, y, mean (SD, range)	25.6 (11.7, 8–56)
Diagnostic delay in years, mean (SD, range)	5.6 (9.1, 0–50.8)
PNES frequency per month, mean (SD, range)	21.9 (61.8, 0.2–450)
Education in years, mean (SD, range)	13.1 (2.7, 7–22)
Marital status, n (%)	
Married/partner	23 (43.4)
Single/separated	30 (56.6)
Employment, n (%)	
Employed/student	23 (43.3)
Unemployed	25 (47.2)
Psychiatric history for anxiety or depression, n (%)	32 (60.4)
Psychotherapy prior to inclusion, n (%)	35 (66.0)
QoL-VAS (n = 49), mean (SD, range)	51.9 (19.3, 20–100)
Attachment styles (ASQ), mean (SD, range)	
Confidence	32.3 (7.3, 19–47)
Attachment anxiety	
Need for approval	26.2 (8.2, 10.0–40.6)
Preoccupied with relationships	28.5 (8.6, 11–47)
Avoidant attachment	
Discomfort with closeness	36.6 (9.8, 16.7–55)
Relationships as secondary	17.6 (7.0, 7–39)
Parental bonding (PBI)	
Paternal PBI dimensions, mean (SD, range)	
care	21.7 (9.5, 3–36)
control	13.9 (7.7, 2–36)
Paternal parenting style, n (%)	
affectionless control (low care, high control)	20 (37.7)
affectionate constraint (high care, high control)	5 (9.4)
neglectful (low care, low control)	8 (15.1)
optimal parenting (high care, low control)	19 (35.8)
Maternal PBI dimensions, mean (SD, range)	
care	25.0 (9.3, 6–36)
control	13.8 (8.4, 0–32)
Maternal parenting style, n (%)	
affectionless control (low care, high control)	15 (28.3)
affectionate constraint (high care, high control)	20 (37.7)
neglectful (low care, low control)	3 (5.7)
optimal parenting (high care, low control)	13 (24.5)
Dissociation (DES), mean (SD, range)	
total	15.9 (11.1, 0–46.8)
Amnesic dissociation	8.0 (9.5, 0–45)
Absorption and imaginative involvement	22.8 (15.7, 0–55.6)
Depersonalization and derealization	10.1 (12.2, 0–58.3)
Somatoform dissociation (SDQ-20), mean (SD, range)	32.1 (8.6, 21–58)
Trauma history (TEC), (n = 52), n (%)	
Emotional trauma	37 (71.2)
Sexual trauma	20 (38.5)
Bodily threat	36 (69.2)
Any trauma	45 (84.9)

dence score of the normative adult population sample was 44.8 (SD = 5.1) for. 29 (56 %) patients had a confidence score \leq 34.6, that is 2 SD below the normative mean [40].

Among our participants, 13 (25 %) rated their mothers as having been an optimal parent and 19 (36 %) provided this rating for their fathers. Comparisons between the dimensions care and control of the parental bonding in our PNES sample and the general population, indicated similar levels of maternal and paternal care and control [41].

At follow-up, 20 of the 51 patients whom we were able to contact (39 %) were free of PNES and 42 (82 %) had a \geq 50 % reduction of seizure (PNES) frequency.

We found significant group-level differences between those patients who had become PNES free and those who had not, concerning reduced healthcare contact ($p = 0.001$) (Table 3).

Patients who were seizure (PNES) free at follow-up had previously reported lower levels of attachment anxiety than those still having PNES ($p = 0.01$) (Table 3).

When comparing patients that achieved a seizure-reduction \geq 50 % at follow-up to those that did not have a reduction in seizure frequency, there were no significant differences concerning attachment styles or perceived parenting.

We used logistic regression analysis to identify independent factors associated with PNES free outcome. Due to our small sam-

ple size, we limited the number of potential predictors and included attachment anxiety (need for approval), sex, and age at PNES onset in the model. Seizure freedom at follow-up was best predicted by male gender; see Table 4.

4. Discussion

In this study, we examined associations between attachment styles and parental bonding, and long-term outcomes among patients with PNES and attempted to identify prognostic factors.

At an average follow up of 5.8 years, 61 % of the patients continued having PNES, based on follow-up data from 96 % of the initially enrolled cohort in our prospective cohort study. The high follow-up rate might reflect the high trust in the Norwegian healthcare system, in general, and, specifically, our center's structured diagnostic and follow-up procedures [42].

Previous studies suggesting poor outcome have been mainly retrospective in nature, some with low responder rates [8–12]. One prospective study reported 66 % of patients still having PNES after 3 years; however, 64 % of the initially enrolled cohort was lost to follow-up [43]. Our data suggest that, despite methodological differences, these previous estimates of outcome may have been realistic.

Table 3
Baseline and follow-up data by PNES outcome, * $p \leq 0.01$.

	PNES – seizure free (n = 20)	PNES – continued (n = 31)	P value
Baseline			
Female sex, n (%)	14 (70 %)	30 (96.8 %)	0.007*
Age at inclusion, mean (SD, range)	30.0 (11.9, 17–52)	34.2 (14.5, 16–62)	0.24
Follow-up time in years, mean (SD, range)	6.3 (2.3, 3.2–9.6)	5.7 (2.5, 1.9–10.9)	0.39
Age at PNES onset, mean (SD, range)	22.5 (9.7, 9–43)	27.9 (12.8, 8–56)	0.11
Diagnostic delay in years, mean (SD, range)	6.0 (7.2, 0.3–25.3)	5.6 (10.5, 0.0–50.8)	0.43
PNES frequency at baseline, monthly, mean (SD, range)	35.9 (98.7, 1–450)	13.2 (14.5, 0.2–70)	0.21
QoL, mean (SD, range)	56 (20.0, 30–100)	49 (19.4, 0–90)	0.27
Education in years, mean (SD, range)	13.2 (3.6, 7–22)	13 (2.1, 10–17)	0.82
Employed or student, n (%)	10 (55.6)	12 (42.9)	0.4
ASQ Confidence, mean (SD, range)	33.3 (7.4, 21.7–47.0)	31.9 (7.3, 19–44)	0.52
ASQ Attachment anxiety (Need for approval), mean (SD, range)	22.6 (7.3, 10–38)	28.5 (8.3, 10–40.6)	0.01*
ASQ Attachment anxiety (Preoccupied with relationships), mean (SD, range)	26.3 (8.3, 12–45)	30.0 (8.7, 11–47)	0.14
ASQ Avoidant attachment (Discomfort with closeness), mean (SD, range)	36.0 (11.3, 16.7–55.0)	36.6 (9.0, 22–53)	0.84
ASQ Avoidant attachment (Relationships as secondary), mean (SD, range)	15.6 (6.2, 7–28)	19.2 (7.3, 8–39)	0.08
Paternal care, mean (SD, range)	24.8 (8.0, 8–35)	19.6 (10.2, 3–36)	0.06
Paternal control, mean (SD, range)	10.9 (7.4, 2–29)	16.1 (7.5, 5–36)	0.02
Maternal care, mean (SD, range)	28.3 (7.6, 9–36)	22.8 (10.2, 6–36)	0.04
Maternal control, mean (SD, range)	12.0 (9.2, 0–31)	14.9 (7.9, 5–32)	0.25
SDQ total, mean (SD, range)	30.6 (6.7, 21–44)	32.7 (9.6, 22–58)	0.41
DES total, mean (SD, range)	13.5 (11.2, 1.4–46.8)	16.6 (10.9, 0–42.5)	0.33
Any trauma in history, n (%)	18 (90)	28 (93)	0.57
Psychotherapy prior to inclusion, n (%)	14 (77.8)	19 (65.5)	0.37
Follow-up			
QoL, mean (SD, range)	74 (18.3, 30–100)	58 (15.5, 0–90)	0.02
Seizure related contact with health care within the last year, n (%)	0	12 (40)	0.001*
Emergency room visits within the last year, n (%)	0 (0)	9 (30)	0.007*
Employed or student, n (%)	10 (50)	14 (45.2)	0.11

Table 4
Potential predictors of PNES-free outcome at follow-up in patients with PNES (multivariate logistic regression analysis), $p \leq 0.05$, Nagelkerke $R^2 = 0.46$.

	Univariate screen		Multivariate model	
	Odds ratio (Confidence Intervals)	P value	Odds ratio (Confidence Intervals)	P value
Age at PNES onset	0.96 (0.91–1.01)	0.12	0.89 (0.82 – 0.98)	0.01*
Attachment anxiety (Need for approval)	0.91 (0.84–0.98)	0.02*	0.91 (0.83 – 0.99)	0.04*
Male sex	12.82 (1.41–111.11)	0.02*	32.26 (2.20–500)	0.01*

In the present study, gender and attachment anxiety were associated with PNES-free outcome. Illness duration, work and educational status, marital status, adverse life-event burden, and levels of dissociation were apparently not associated with outcome. The non significance of traumatic life events on the prognosis in our study could be due to the high rates of recorded adverse life-event burden in both groups (93 % and 90 %), that could mitigate possible differences.

Nevertheless, levels of secure attachment were significantly lower than those reported from a normative sample [40]. Our findings showed an inverse association between attachment anxiety and remission of PNES at follow-up after a mean of 5.8 years. Attachment anxiety was a negative predictor of a PNES-free outcome in the multivariate regression analysis, but the odds ratio (OR) was low.

Insecure and disorganized attachment styles have previously been linked to psychiatric conditions [44], including functional neurological disorders [45]. In patients with PNES, fearful attachment [23] and insecure attachment [24] have been found to be the predominant attachment styles. Attachment patterns might also play a role in the therapeutic process and influence outcome [25]. Patients with anxious attachment have been described as being difficult to treat, often presenting with chaotic and contradictory representations of self and others [25]. In patients with borderline personality disorder, it has been shown that those having a preoccupied attachment style were more likely to not respond to intervention. It has been argued that preoccupied attachment style might complicate the engagement in the therapeutic treatment and the alliance with the therapist [46].

Another concept that might be closely related is that of defense styles. It has been argued that patients with PNES might have different underlying psychopathology and defense mechanisms which again could influence prognosis [27]. Defense mechanisms are commonly categorized in mature, neurotic, and immature styles [47]. Whereas mature defense style comprises normal and adaptive mechanisms of coping with troubling situations, both neurotic and immature styles are seen as dysfunctional and maladaptive coping strategies [48]. Patients with PNES are likely to use less mature defensive strategies, which again might be associated with insecure attachment patterns [49].

To explore a patient's attachment pattern might be useful for tailoring their therapeutic strategies.

In our study, 35.8 % of our patients with PNES described their fathers as an optimal caregiver during childhood, and even fewer (24.5 %) characterized their mothers as optimal parents. Optimal parenting is delineated by high care and low control. Recollections of parenting style were not found to be associated with remission of PNES seizures at follow-up in our study. It has been shown that the type of parenting received from both the mother and the father influences psychological wellbeing in adulthood [50]. Perceived parental care and control have also been associated with mental disorders in adolescence [16]. A study of a pediatric cohort with PNES found no difference in perceived parenting between patients with PNES and their siblings [19].

In our study, being male was the strongest predictor of a good (i.e., PNES-free) outcome. The numbers were small, with only 8 males in the cohort and the results have large confidence intervals, indicating low precision of the OR. Whether gender may, nevertheless, influence PNES outcome can be debated. Previous studies have yielded contradictory results, with one finding male gender being predictive of a favorable outcome [51], whereas another study found that female gender was predictive of a good outcome [52]. Men are under-represented in most studies of PNES, and therefore may have gender differences in patients with PNES been

insufficiently studied. From studies that have examined gender differences, we know that men experience significantly less sexual traumas and show lower levels of dissociation than women [53]. Both these factors could play a role in PNES severity and outcome.

A lower age at PNES onset was not associated with a PNES-free outcome in the univariate analysis in our cohort. In the multivariate analysis, however, it was a predictor of favorable outcome, but with a low OR. Some previous studies have found that younger age at PNES onset is favorable for recovery [8,10]. Different etiopathological mechanisms in pediatric and adult populations with PNES have been hypothesized as being possible reasons for such age-related differences in prognosis.

Self-reported overall health scores (QoL-VAS) were low compared with values from the general population from Norway [28], and in line with reports from other large PNES cohorts [54], indicating poor quality of life (QoL) in patients with PNES. Persistence of PNES at follow-up was associated with poor QoL, whereas patients who were free of PNES at follow-up reported increased scores for QoL although not reaching statistical significance. Nevertheless, reduction in seizure frequency was not associated with improved QoL. Similar findings have been reported from other studies on PNES outcome [8]. There has been some debate on treatment goals and outcome measures for patients with PNES. These findings suggest that the impact of treatments that reduce PNES frequency will be of limited value for quality of life and that cessation of PNES seizures remains an important goal in treatment.

In our whole cohort, including the group of the patients with ongoing PNES at follow-up, contact with healthcare services was reduced over time since diagnosis. Indeed, 60 % of patients with persistent PNES reported not having had contact with healthcare services for PNES-related reasons during the year prior to follow-up. Reduction in healthcare expenses following diagnosis of PNES has been reported previously [55].

4.1. Strengths and limitations

The main strength of our study is the follow-up after a prolonged period, and the very low rate of patients that were lost to follow-up. Only patients with documented PNES, according to the ILAE recommendations, were included in our study and we defined PNES remission as freedom of PNES for the duration of at least one year.

Although we were able to study as many as 53 patients from our national tertiary care center for an average follow-up period of almost six years, our study is under-powered: the number of includable cases fell short of the calculated minimum sample size. The size of our sample also limited the numbers of potential predictors to be studied.

Another limitation in our study is that, although prospective, we were not able to control for all factors/events to which the patients were exposed prior to follow-up. In addition, our cohort was recruited from a single tertiary epilepsy center with an established diagnostic and follow-up pathway for patients with PNES, and this may restrict the generalizability of our findings.

Studies of predictive factors for PNES outcome have shown inconsistent results, and larger prospective (multi-center) studies are necessary to explore this further.

5. Conclusion

The long-term prognosis of PNES in our cohort from a tertiary epilepsy center is poor. Attachment anxiety is a risk factor for persistent PNES. It may be of therapeutic relevance to assess attachment patterns in patients with PNES.

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Declaration of Competing Interest

Author AV has served as a paid consultant for Eisai and Arvelle Therapeutics, unrelated to this study. Author RD receives royalties from UpToDate. Author MIL has served as a paid consultant for Eisai, UCB and Arvelle Therapeutics, unrelated to this study. Author CL has no conflicts of interest to disclose.

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