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Short-term effect of inpatient treatment of psychogenic non-epileptic seizures

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ABSTRACT

INTRODUCTION. Psychogenic non-epileptic seizures (PNES) is a dissociative disorder with attacks resembling epileptic seizures. Previous studies have shown that patients with PNES have distinct demographical and health-related features. No studies, however, exist that describe Danish patients with PNES. In this study, we present the clinical characteristics of patients who received inpatient cognitive behavioural psychotherapy for PNES. We also present data on the short-term effect of PNES treatment for patients with and without comorbid epilepsy.

METHODS. In this retrospective study, we reviewed medical records for patients admitted for treatment of PNES at the Danish Epilepsy Centre from 2018 to 2023. We compared psychometric scores before and after admission as outcome measures.

RESULTS. Our cohort consisted of 86.6% women with a mean age of 34.1 years at admission. 29.1% lived alone, and only 39.6% were employed or under education. The patients had a long history of PNES (mean 68.6 months), and a large proportion had comorbid epilepsy (34.1%) or psychiatric comorbidity (67.2%). We found significant improvement in all psychometric scores after admission. Comorbid epilepsy had no significant impact on this effect.

CONCLUSIONS. Danish patients receiving inpatient treatment for PNES are very similar to other published cohorts. Four weeks of psychotherapy significantly improved all psychometric scores for patients both with and without epilepsy.

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TRIAL REGISTRATION. Not relevant.

Psychogenic non-epileptic seizures (PNES) are attacks that mimic epileptic seizures but are without a physiological explanation. The best term for the condition remains debated, but we use the term PNES. The diagnosis is often elusive and requires neurological and neurophysiological expertise. The cornerstone of the diagnosis remains video-electroencephalography (video-EEG), which, in the case of PNES, is normal during seizures [1]. PNES is a relatively common disorder with an estimated prevalence of 2-33/100,000 [2].

In the international classification of diseases, PNES is defined as a dissociative disorder [3] and over the past decades, psychotherapy has emerged as a treatment modality with some effect [4]. Cognitive behavioural therapy (CBT), in particular, seems to be useful [5]. The evidence for effect on long-term seizure cessation is limited, but several studies show a higher quality of life after psychotherapeutic treatment [6, 7].

CBT can be provided in an outpatient or an inpatient setting, but the scientific evidence is limited, especially for inpatient treatment. The few existing studies show a significant benefit of CBT in terms of seizure reduction and improvement of psychometric scores [8-10]. No Danish studies on inpatient treatment of PNES have been published.

This paper reports the clinical characteristics of a cohort of patients who received inpatient therapy for PNES at the Epilepsy Hospital in Denmark. We also investigate the effect of inpatient CBT on PNES in a Danish context using psychometric tests as an outcome measure. We include an assessment of the impact of comorbid epilepsy on that effect, a topic that has been speculated to be important [10] but remains uninvestigated.

Methods

The investigation was conducted as a quality control and development study. Therefore, all data used in the study were collected retrospectively, and all interventions described were performed for clinical purposes. The study was approved by the management at the Danish Epilepsy Centre, which is the only requirement for this type of study in Denmark.

Study population

All patients admitted for inpatient treatment of PNES aged 18 years and older from 1 January 2018 to 31 December 2023, who underwent assessment with psychometric scores, were evaluated for participation. In a very limited number of admissions, psychometric scoring was not conducted. Since no data was available for these patients, they were excluded from the analyses.

Data collection

All data were collected retrospectively by review of patient files and other digital systems. Immediately after export from the systems of origin, the data were controlled for inconsistencies and errors. After all queries had been resolved, data were irrevocably anonymised.

All data were collected without patient consent in accordance with the Danish Health Act ("Sundhedsloven"), Section 42 d.

We collected demographical data, information on the diagnoses of interest (PNES, epilepsy and psychiatric comorbidity) and relevant social factors.

Intervention

All patients were treated during a four-week admission at the Danish Epilepsy Centre in Dianalund, Denmark. For logistics reasons, the Danish Epilepsy Centre does not provide outpatient treatment; therefore, there was no selection of patients for inpatient versus outpatient therapy. A psychiatrist evaluated all patients before admission.

During hospitalisation, patients participated in 3-5 daily therapeutic activities with breaks for rest and reflection in an open environment and were encouraged to share their experiences. Patients stayed at the ward from Monday to Friday and spent weekends at home.

The overall approach of the intervention during admission is based on CBT, but since that is not a precisely defined term, **Table 1** summarises the specific interventions provided during admission.

TABLE 1 Specific interventions and assessments conducted as part of the treatment of PNES during admission at the Danish Epilepsy Centre.

Specific intervention	Intervention type	Duration, min.	Frequency
Cognitive body therapy	Individual	60	1/week
Cognitive behavioural therapy	Individual	60-150	1-2/week
Sensory awareness therapy	Individual	30	1/week
Exercise	Group	30-60	1/week
Psychoeducation	Group	60-120	1-2/week
Mindfulness	Group	45-60	1/week
Psychiatric assessment	Individual	60	1 × at admission
Psychometric scores	Individual	60	At admission and discharge
Sessions with primary caregiver	Individual	15-60	As needed, min. 1/week
Discharge preparation sessions	Group	60-90	3 sessions in the last week of admission
Life structure and energy management			
Relapse handling			
Coping mechanisms			
Social activities	Group	15-30	5/week

PNES = psychogenic non-epileptic seizures.

The nursing staff members had received no less than one year of education in cognitive therapy methods. Psychometric scoring was conducted as part of the routine procedures within three days after admission and again within three days prior to discharge.

Outcome measures

The battery of health assessment scales comprised the Beck Depression Inventory II (BDI-II), the Beck Anxiety Inventory (BAI), the Quality Of Life In Epilepsy 31 (QOLIE-31), the Perceived Stress Scale (PSS-10) and the Brief Illness Perception Questionnaire (B-IPQ). Please see the supplementary material for a more detailed description (Appendix 1) and example questionnaires (Appendix 1A-1E). All questionnaires are available in Danish and have been validated.

Statistical analyses

Statistical analyses were conducted using JASP 16.1. For comparison of psychometric scores before and after admission, we used a repeated measures ANOVA with time (PRE versus POST) as a two-level within-subjects factor and comorbid epilepsy as a between-subjects grouping factor. Post-hoc analyses and sphericity testing were not possible for the within-subjects factor (only two levels). Still, we conducted post-hoc analyses on the epilepsy time interaction term for each outcome score with Bonferroni correction for multiple comparisons. We used ω^2 as a measure of statistical effect size.

Trial registration: not relevant.

Results

In total, 154 admissions were screened for eligibility. Among these, 20 admissions were excluded as they were either interrupted or extended. Altogether, we included 122 unique patients with 134 admissions. A total of 35 patients had been admitted more than once. These numbers do not add up because some admissions occurred outside our study's time scope.

Table 2 summarises our findings in terms of descriptive statistics.

TABLE 2 Psychosocial and epilepsy/PNES-related characteristics of patients who received inpatient treatment for PNES at the Danish Epilepsy Centre.

	PNES only	PNES and epilepsy	Total
Admissions, n (%)			
1 admission	89 (65.9)	45 (34.1)	134 (100)
≥ 1 admissions	-	-	35
Age at admission, mean (± SD; min.-max), yrs	32.7 (± 14.2;18-86)	36.9 (± 12.1;19-62)	34.1 (± 13.7; 18-86)
Sex, n (%)			
Male	13 (14.6)	5 (11.1)	18 (13.4)
Female	76 (85.4)	40 (88.9)	116 (86.6)
Duration of PNES before admission, mean (± SD; min.-max), mos.	76.4 (± 81.6; 4-360)	53.0 (± 45.9; 4-172)	68.6 (± 72.3; 4-360)
Previous treatment for PNES, n (%)			
None	49 (55.1)	27 (60.0)	76 (56.7)
Outpatient only	21 (23.6)	2 (4.4)	23 (17.1)
Inpatient only	10 (11.2)	8 (17.8)	18 (13.4)
Both	9 (10.1)	8 (17.8)	17 (12.7)
Current psychiatric comorbidity, n (%)	59 (66.3)	31 (75.6)	90 (67.2)
Currently employed or in education, n (%)	38 (42.7)	15 (33.3)	53 (39.6)
Living alone, n (%)	25 (28.1)	14 (31.1)	39 (29.1)
Diagnostic certainty: PNES, n (%)			
Confirmed	57 (64.0)	34 (75.6)	91 (67.9)
Clinical	20 (22.5)	8 (17.8)	28 (20.9)
Probable	12 (13.5)	3 (6.7)	15 (11.2)

PNES = psychogenic non-epileptic seizures; SD = standard deviation.

Please see the supplementary material for further clarification of the definitions used in Table 2 (Appendix 2). Details on the distribution of specific psychiatric diagnoses are also available (Appendix 3, Table 1S).

Concerning the effect of the inpatient treatment programme, we found a significant difference in all the psychometric scores from admission to discharge. **Table 3** summarises our findings on the effect, including separate post-hoc analyses for patients with PNES only and patients with PNES + epilepsy.

TABLE 3 Values for each outcome score at admission and discharge for patients with PNES only and patients with PNES + epilepsy, and as grand mean (both groups together). All changes were significant in the repeated measures ANOVA. Statistical effect size is small to medium for the BAI, medium for the QOLIE-31 and the PSS-10, and medium to large for the BDI-II and the B-IPQ.

	Outcome score, mean (± SD)		F statistic:		
	at admission	at discharge	df 1,132	p value	Effect size, ω^2
B-IPQ[a]					
PNES only	48.93 (± 11.19)	38.00 (± 14.26)	-	< 0.001	-
PNES + epilepsy	48.47 (± 8.47)	40.69 (± 13.44)	-	< 0.001	-
Grand mean	48.78 (± 10.32)	38.90 (± 13.99)	67.32	< 0.001	0.113
BDI-II[b]					
PNES only	19.03 (± 12.73)	11.01 (± 10.13)	-	< 0.001	-
PNES + epilepsy	21.78 (± 14.44)	12.78 (± 12.77)	-	< 0.001	-
Grand mean	19.96 (± 13.34)	11.60 (± 11.01)	90.54	< 0.001	0.097
BAI[c]					
PNES only	23.40 (± 15.80)	17.06 (± 13.47)	-	< 0.001	-
PNES + epilepsy	23.87 (± 14.36)	17.98 (± 13.75)	-	0.002	-
Grand mean	23.56 (± 15.28)	17.37 (± 13.52)	39.70	< 0.001	0.038
QOLIE-31[d]					
PNES only	37.16 (± 13.62)	44.78 (± 15.27)	-	< 0.001	-
PNES + epilepsy	37.36 (± 11.05)	45.62 (± 11.42)	-	< 0.001	-
Grand mean	37.22 (± 12.77)	45.06 (± 14.06)	99.85	< 0.001	0.072
PSS-10[e]					
PNES only	19.65 (± 10.64)	14.51 (± 9.57)	-	< 0.001	-
PNES + epilepsy	23.18 (± 9.63)	16.98 (± 9.19)	-	< 0.001	-
Grand mean	20.84 (± 10.41)	15.34 (± 9.48)	83.97	< 0.001	0.068

B-IPQ = Brief Illness Perception Questionnaire; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory II; df = degrees of freedom; PNES = psychogenic non-epileptic seizures; SD = standard deviation; QOLIE-31 = Quality Of Life In Epilepsy 31; PSS-10 = Perceived Stress Scale 10.

a) 0-80, lower is better.

b) 0-63, lower is better.

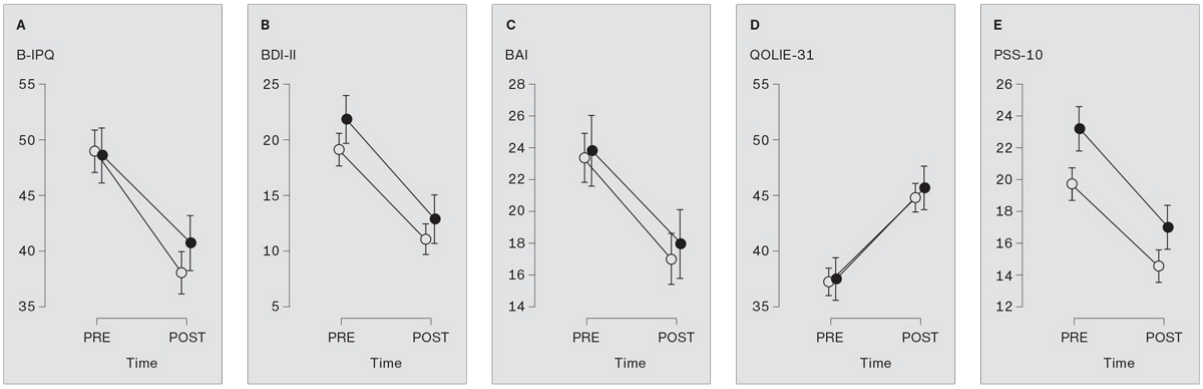
c) 0-63, lower is better.

d) 11-73, higher is better.

e) 0-40, lower is better.

We found no significant interaction between the presence of epilepsy and the change in scores over time for any outcome measures. This means that whether the patients had epilepsy or not did not significantly affect the impact of their PNES treatment. **Figure 1** visualises the relations between the effects of treatment over time and the presence of comorbid epilepsy.

FIGURE 1 The results of the repeated measures ANOVA illustrate the effect of inpatient psychotherapy for each of the psychometric outcome scores (mean ± standard deviation) for patients with and without epilepsy. The nearly parallel lines in most panels demonstrate that there was no significant difference in the effect of the treatment between patient groups for any of the outcome scores. In panel A, the noticeably different slope between the lines indicates some difference in the effect of CBT between groups, but this difference was not statistically significant. The noticeable distance between the lines in panel E indicates a near-significant difference between groups. **A**. Brief Illness Perception Questionnaire (B-IPQ: 0-80, lower is better). **B**. Beck Depression Inventory II (BDI-II: 0-63, lower is better). **C**. Beck Anxiety Inventory (BAI: 0-63, lower is better). **D**. Quality Of Life In Epilepsy 31 (QOLIE-31: 11-73, higher is better). **E**. Perceived Stress Scale 10 (PSS-10: 0-40, lower is better).



PRE = before admission; POST = after admission.

Discussion

The purpose of this study was three-fold. Firstly, to provide clinical characteristics on a Danish cohort of patients who received inpatient CBT for PNES. Secondly, to inform on the short-term effect of CBT on PNES using psychometric scores as an outcome measure. Thirdly, to evaluate whether comorbid epilepsy affected the impact of CBT on PNES.

As an outcome measure, the frequency of PNES is commonly used. Unfortunately, psychogenic seizures were not recorded in detail, and seizure frequency was therefore unavailable as an outcome measure. It has, however, been proposed that psychometric scores may be a better measure of the impact of PNES on patients' quality of life [11]. Therefore, we opted to use all available psychometric scores as outcome measures.

We presented a cohort of 122 patients. To our knowledge, this is the largest published cohort for inpatient treatment of PNES. On the first objective, we found that in most respects, our cohort was similar to those presented in other studies, with a large proportion being women (70-86%), a mean age at diagnosis or treatment onset between 30-35 years, less than 50% being employed or in education and a mean 6-9-year PNES duration at treatment onset. In the supplementary material, we provide a table (**Appendix 4, Table S2**) summarising several previous studies on PNES [8-10, 12-16] for comparison. Psychiatric comorbidity is an area of interest in studies on PNES. A meta-analysis from 2016 by Diprose et al. found rates of psychiatric comorbidity ranging from 53 to 100%, with the most notable diagnoses being post-traumatic stress disorder (PTSD), personality disorders, depression and anxiety [17]. This is in line with our findings of 67.2% overall. Interestingly, we also found that attention deficit with or without hyperactivity (ADHD/ADD) was a frequent psychiatric comorbidity. This additional finding may be explained by a generally increased awareness of ADHD/ADD in recent years, leading to an increase in ADHD/ADD diagnoses [18].

On the second and third objectives, we found a significant effect of inpatient CBT at discharge across all the scores. This applied to patients with PNES + epilepsy (P+E) and patients with only PNES (P-only). This implies

that the same CBT intervention can be used for patients with PNES regardless of the presence of comorbid epilepsy.

The Beck Depression Inventory (BDI-II) revealed a small difference between P+E and P-only groups. Still, it was not significant, and no significant difference was observed in the effect of CBT between groups. Commonly used cut-off scores translate these improvements from mild to moderate depression (14-19/20-28) to normal/minimal depression (0-13). In previous studies on inpatient treatment of PNES, Labudda et al. [10] and Kuyk et al. [9] found very similar mean BDI-II scores at both admission and discharge across both patient groups. This indicates that our population had a similar degree of psychopathology (regarding depression) before CBT and that the CBT we employed had a very similar effect on depression symptoms. This is noteworthy since the treatment period was considerably longer in the studies by Labudda et al. [10] and Kuyk et al. [9] (means of 64.53 days and 4.8 months, respectively). This suggests that, regarding depression symptoms, longer treatment periods do not necessarily improve the outcome beyond a certain threshold.

For the Beck Anxiety Inventory (BAI), the difference between P+E and P-only groups was very small, and the effect of CBT was very similar. Using the common cut-off scores, the reduced scores all fall within the “moderate anxiety” interval (16-25), which may indicate that despite the statistical significance of the improvement, it may not be clinically relevant. In previous studies, Kuyk et al. [9] and Labudda et al. [10] used the State-Trait Anxiety Inventory - Trait (STAI-T) as a measure of anxiety, and direct comparison is therefore not meaningful. They did, however, also find significant improvements after inpatient CBT. This discussion demonstrates the challenges of using different psychometric scores. It would be of great benefit to future research to develop a standard test battery.

For the Perceived Stress Scale (PSS-10), we found some differences between P+E and P-only groups, with P+E having the higher scores. The difference, however, was not statistically significant. The effect of CBT in either group was almost the same. In both groups, the mean scores before and after CBT remained within the established “moderate perceived stress”-interval (14-26), suggesting limited clinical relevance.

Limitations

The main limitation of this study was its retrospective design, which restricted the available data. For instance, we lacked a well-defined seizure frequency as a supplementary outcome measure. Another shortcoming is the lack of follow-up data after discharge (e.g. after 3, 6 or 12 months). Therefore, the extent to which the effect of the treatment transfers to real-life situations and the duration of its sustainability remains unclear.

A second concern is the lack of data from patients who did not complete the outcome scorings. For reasons unknown, a few patients did not complete the scorings. By our best estimate, this group comprises no more than 10-15 patients. It seems unlikely that these few patients would significantly change the overall characteristics or outcome estimates, but we cannot exclude the possibility entirely.

A final limitation is the limited number of patients included. While we included more patients than other studies on inpatient PNES treatment, data remained too limited to conduct statistically valid subgroup analyses.

Conclusions

In this study, our cohort of 122 patients who received inpatient treatment for PNES comprised mainly younger women, of whom 67% had psychiatric comorbidity, and approximately 40% were employed or in education. Overall, our cohort was similar to other published cohorts.

In addition, we found significant improvement in various psychometric scores after four weeks of inpatient

treatment with CBT. This improvement is in line with previous studies, but we found this effect in a considerably shorter time than was previously observed. We found no significant difference in the effect of CBT between patients with PNES only and those with both PNES and epilepsy.

Agreement on a minimum psychometric test battery would enhance cross-study comparisons and meta-analyses.

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