RESEARCH ARTICLE

Psychiatric Disorders in Children and Adolescents With Psychogenic Nonepileptic Seizures

Anne Sofie Hansen, MD, Charlotte Ulrikka Rask, MD, PhD, Ann-Eva Christensen, PhD, Maria Rodrigo-Domingo, PhD, Jakob Christensen, MD, PhD, DrMedSci, and René Ernst Nielsen, MD, PhD

Correspondence
Dr. Hansen
ansoha@rn.dk

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Abstract

Objective

Knowledge regarding psychiatric disorders in children and adolescents with psychogenic nonepileptic seizures (PNES) is limited. This study outlines the spectrum and risk of psychiatric disorders in childhood-onset PNES.

Methods

We performed a nationwide matched cohort study of children and adolescents with PNES 5 to 17 years of age at the time of diagnosis between January 1, 1996, and December 31, 2014. Two matched comparison groups were included: children and adolescents with epilepsy (ES) and children and adolescents without PNES or epilepsy, called healthy controls (HC). Outcomes were prevalent psychiatric disorders before index (i.e., date of diagnosis or corresponding date for HC) and incident psychiatric disorders 2 years after index. Relative risks (RRs) were calculated and adjusted for potential confounders.

Results

We included 384 children and adolescents with validated PNES, 1,152 with ES, and 1,920 HC. Among the cases of PNES, 153 (39.8%) had prevalent psychiatric disorders and 150 (39.1%) had incident psychiatric disorders. Compared to the ES and HC groups, children and adolescents with PNES had elevated risks of both prevalent psychiatric disorders (adjusted $RR_{PNES/ES}$ 1.87, 95% confidence interval [CI] 1.59–2.21, adjusted $RR_{PNES/HC}$ 5.54, 95% CI 4.50–6.81) and incident psychiatric disorders (adjusted $RR_{PNES/ES}$ 2.33, 95% CI 1.92–2.83, adjusted $RR_{PNES/HC}$ 8.37, 95% CI 6.31–11.11). A wide spectrum of specific psychiatric disorders displayed elevated RRs.

Conclusions

Children and adolescents with PNES are at higher risk of a wide range of psychiatric disorders compared to children and adolescents with ES and HC. A careful psychiatric evaluation is warranted to optimize and individualize treatment.

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From Psychiatry (A.S.H., A.-E.C., M.R.-D., R.E.N.), Aalborg University Hospital; Department of Clinical Medicine (A.S.H., R.E.N.), Aalborg University; Department of Child and Adolescent Psychiatry (C.U.R.), Research Unit, and Department of Neurology (J.C.), Aarhus University Hospital; and Department of Clinical Medicine (C.U.R., J.C.), Aarhus University, Denmark.

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Glossary

ADD = attention-deficit disorder; **ADHD** = attention-deficit/hyperactivity disorder; **ASD** = autism spectrum disorder; **CI** = confidence interval; **ES** = epilepsy; **HC** = healthy controls; **ICD** = *International Classification of Diseases*; **PNES** = psychogenic nonepileptic seizures; **PPV** = positive predictive value; **RR** = relative risk; **SSRD** = somatic symptom and related disorders.

Psychogenic nonepileptic seizures (PNES) present with intermittent involuntary movements, changes in consciousness, or loss of self-control that can mimic epileptic seizures but without the characteristic semiology and ictal epileptiform activity on EEG found in persons with epileptic seizures.[1,2] The diagnostic assessment is often challenging and can result in a misdiagnosis of epilepsy (ES) and a subsequent delay of PNES diagnosis.[3] The prolonged time to correct diagnosis can cause distress and impairment of daily functioning for the affected patients and their families.[4] Even when patients receive the correct diagnosis, lack of collaborative care between the somatic and mental health departments is common, despite an acknowledged link between PNES and psychiatric disorders.[5,6] Multidisciplinary management with an integrated psychiatric assessment and psychotherapy is the recommended standard of care.[7-10] Previous research has suggested that emotional disorders and adjustment disorders are common in children and adolescents with PNES.[1,2] However, recent studies indicate an occurrence of a wider spectrum of psychiatric disorders, including neurodevelopmental disorders.[6,11-15]

At present, existing studies comprise mainly adult or small pediatric populations recruited from highly specialized treatment units, with no large-scale population-based studies addressing the full range of psychiatric disorders in children and adolescents diagnosed with PNES. Thus, the full range of psychiatric disorders present in children and adolescents with PNES is inadequately described, and further knowledge is needed to qualify multidisciplinary management.

The aim of the current study is twofold: (1) to describe the spectrum of psychiatric disorders in children and adolescents diagnosed with PNES, both before the PNES diagnosis and during a 2-year follow-up period after the PNES diagnosis, and (2) to examine the risk of psychiatric disorders in those with childhood-onset PNES compared to matched children and adolescents with ES and to matched controls without PNES or ES.

Methods

Study Design and Data

We performed a nationwide register-based cohort study of children and adolescents 5 to 17 years of age living in Denmark and registered with an incident diagnosis of PNES during the inclusion period between January 1, 1996, and December 31, 2014. Patients with PNES were matched to (1) a population of children and adolescents with onset of ES and (2) a population of children and adolescents without PNES or ES, called healthy controls (HC). All individuals were followed up for 2 years after inclusion (censoring at death or immigration from Denmark).

Each individual in Denmark is assigned a unique personal identification number at birth or immigration (the Civil Person Registration number), which was used to link individual information from a range of nationwide health and social registers. Information on diagnoses registered in context with inpatient and outpatient hospital contacts was retrieved from the Danish National Patient Register[16] and the Danish Psychiatric Central Research Register[17] for all included children and their parents. The Danish National Patient Register covers somatic inpatient contacts from 1977 with outpatient contacts and emergency room visits included since 1995. The Danish Psychiatric Central Research Register covers psychiatric inpatient contacts from 1970 with outpatient contacts and emergency room visits included from 1995.

Data on parental educational level were retrieved from the Danish Population Education Register.[18] Parental information was included as covariate information for the data analyses as described below.

Study Population

PNES Cases

We identified all children and adolescents 5 to 17 years of age registered with a diagnosis of dissociative seizures (ICD-10: F44.5) or other and unspecified convulsions, nonepileptic seizures (ICD-10: R56.8G) in the Danish health care registers during the inclusion period. Individuals diagnosed before December 31, 1995, with a possible PNES disorder (ICD-8: 300, 305, 306, 307, 308, 780; or ICD-10: F44.5, F91.8, F98.9, R56.8) were excluded to ensure incident cases only. Furthermore, individuals registered with solely an inclusion diagnosis (ICD-10: F44.5 or R56.8G) at an emergency department were excluded. We validated the PNES diagnosis for each included individual according to an adapted version of the International League Against Epilepsy criteria using clinical information from medical records.[19] A detailed description of the validation process has been supplied previously.[20] All individuals in the PNES population were assessed for epileptic seizures at the time of inclusion on the basis of existing medical records including information on neuroimaging and EEG. The index date was set as the date of the incident hospital contact with the first registered inclusion diagnosis of PNES as defined above.

ES Controls

We included a comparison group consisting of children and adolescents registered with a diagnosis of ES (ICD-10: G40.x) during the inclusion period matched 3:1 to the PNES population on sex, year of birth, and year of inclusion diagnosis. The index date was set as the date of the incident hospital contact with the first registered inclusion diagnosis of ES.

To ensure that we included only incident cases with ES, children and adolescents with a diagnosis of ES (ICD-8: 345; ICD-10: G40.x) before the inclusion period were excluded. Furthermore, individuals with a possible diagnosis of PNES (ICD-8: 300, 305, 306, 307; ICD-10: F44.5, R56.8G) before their index date were also excluded from the ES controls.

HC Group

The HC group was made up of children and adolescents from the general population matched 5:1 to the PNES population on sex and year of birth. Persons with a diagnosis of PNES (ICD-8: 300, 305, 306, 307; ICD-10: F44.5, R56.8G) or a diagnosis of ES (ICD-8: 345; ICD-10: G40.x) before the corresponding index date of the matched PNES case were not eligible for the HC group.

Outcomes

Psychiatric diagnoses registered before the index date were grouped into diagnostic categories as described below and called prevalent psychiatric disorders. Psychiatric diagnoses registered within 2 years after the index date were grouped similarly and called incident psychiatric disorders when the individual had no registered prevalent psychiatric disorder within the diagnostic category. Individuals with multiple psychiatric disorders were included in the analyses of each corresponding diagnostic category.

According to previous studies in PNES,[1,2,21] we grouped the registered psychiatric diagnoses in the following categories: emotional disorders (i.e., anxiety, obsessive-compulsive disorder, and mood disorders [ICD-10: F30-F39, F40-F42, F93, F98 (excluding F98.8C)]), adjustment disorders (i.e., stress-related conditions, posttraumatic stress disorder, and attachment disorders [ICD-10: F43, F94]), neurodevelopmental disorders (i.e. attention-deficit/hyperactivity disorder [ADHD], attention-deficit disorder [ADD], autism spectrum disorder [ASD], tics/Tourette syndrome, and conduct disorder [ICD-10: F84, F88-F89, F90-F92, F95, F98.8C]), intellectual disorders (ICD-10: F70-F79, F80-F83), somatic symptom and related disorders (SSRD; ICD-10: F44 [excluding F44.5], F45, F48), personality disorders (ICD-10: F60-F61), psychotic disorders (ICD-10: F20-F29), eating disorders (ICD-10: F50), self-harm (ICD-10: X60-X84), and substance use (F10-F19) (table 1 provides corresponding ICD-8 codes).

Two further outcomes were defined for both prevalent and incident psychiatric disorders: any psychiatric disorder was a binary variable identifying the occurrence of any of the above defined psychiatric disorder categories in an individual, and ≥2 psychiatric disorders was a binary variable identifying the occurrence of ≥2 of the above defined psychiatric disorder categories in an individual. In addition, we investigated diagnostic subgroups for 2 diagnostic categories: emotional disorders (i.e., anxiety disorders, mood disorders, and obsessive-compulsive disorder) and neurodevelopmental disorders (i.e., ADHD/ADD, ASD, conduct disorder, and tics/Tourette syndrome) (table 1 provides corresponding ICD-10/ICD-8 codes).

Covariates

Any prevalent psychiatric disorder was defined as a binary variable determined by the prevalence of any psychiatric disorder before the index date as defined above.

Parental history of psychiatric disorders was defined as a binary variable determined by the registration of any psychiatric disorder before the index date in either parent.

Parents' highest level of education was defined as the highest registered completed level of education at the index date for either parent and divided into 4 levels: primary (elementary school), secondary (high school), vocational (skilled), and college (short-, medium-, and long-term education).

Statistical Analyses

Continuous variables are summarized by median and interquartile range, while categorical variables are presented as frequencies and percentages. For each of the outcomes listed above, Poisson regression with robust estimation of the standard error was used to compute relative risks (RRs) of psychiatric disorders with PNES as the reference group.[22] We calculated both crude and adjusted RRs with corresponding 95% confidence intervals (CIs) and reported inverse RRs and CIs for a more intuitive interpretation. For prevalent psychiatric disorders, the models were adjusted for parental history of psychiatric disorders and parents' highest level of education. For incident psychiatric disorders, the models were adjusted for any prevalent psychiatric disorder, parental history of psychiatric disorders, and parents' highest level of education. A Wald test was used for comparison of all 3 groups.

Sensitivity analyses stratified on sex, age at index >12 or <12 years, and coexisting epileptic seizures, and sensitivity analyses on subpopulations consisting of children and adolescents from the PNES population with (1) no comorbid epileptic seizures, (2) a video EEG–validated PNES diagnosis, and (3) children >12 years of age at index were performed.

Statistical analyses were performed with Stata 16 (StataCorp, College Station, TX) on the Statistics Denmark server with remote access. Level of significance was set to 0.05.

Standard Protocol Approvals, Registrations, and Patient Consents

This study was conducted in accordance with Strengthening the Reporting of Observational studies in Epidemiology criteria for observational studies. Study protocol approvals and

Table 1 Definition of Psychiatric Disorder Categories and Subgroups

Psychiatric Disorders	ICD-10 Codes	ICD-8 Codes
Emotional disorders (includes anxiety, OCD and depression, bipolar disorder)	F30–F39 F40–F42 F93, F98 (excluding DF98.8C)	296.x9 (excluding 296.89), 298.09, 298.19, 300.49, 301.19 300.x9 (excluding 300.49, 300.5–300.7)
Adjustment, PTSD, and attachment disorders	F43, F94	307, 308.4
Neurodevelopmental disorders (ASD, ADHD, tics/Tourette, ODD/CD)	F84, F88–F89 F90-F92, F95 DF98.8C	299.00, 299.01, 299.02, 299.03 306.1, 306.x9, 308.xx (excluding 306.1, 306.3, 308.4)
Intellectual and specific learning disabilities	F70–F79, F80–83	311.xx, 312.xx, 313.xx, 314.xx, 315.xx, 306.1
Somatic symptom and related disorders (excluding PNES)	F44.xx (excluding F44.5), F45, F48	300.5–300.7 305.xx (excluding 305.8, 305.9)
Personality disorders	F60, F61	301.x9 (excluding 301.19), 301.80, 301.81, 301.82, 301.84
Psychotic disorders (includes schizophrenia, schizotypal, schizoaffective, and other psychotic disorders)	F20–F29	295.x9, 296.89, 297.x9, 298.29–298.99, 299.04, 299.05, 299.09, 301.83
Eating disorders (includes anorexia nervosa and bulimia nervosa)	F50	306.50, 306.58, 306.59
Self-harm	X60–X84	E950–E959, E980–E989
Substance use	F10–F19	291, 294.3x, 303.x9, 303.20, 303.28, 303.90, 304.x9

Psychiatric Disorder	Subgroups	ICD-10	ICD-8
Emotional disorders	A. Anxiety disorders, including phobic, generalized, and panic anxiety B. Mood disorders C. OCD	A. F40, F 41, F93.1, F93.2, F93.8 B. F30–F39 C. F42	A. 300.0–300.02, 300.4 B. 296.x9 (excluding 296.89), 298.09, 298.19, 300.49, 301.19 C. 300.3
Neurodevelopmental disorders	A. ADHD, ADD B. ASD C. Conduct disorders D. Tic disorders	A. F90, F98.8C B. F84 C. F91 D. F95	A. 308.3 B. 299.00, 299.01, 299.02, 299.03 C. 308.1–308.2 D. 306.2

Abbreviations: ADD = attention-deficit disorder; ADHD = attention-deficit/hyperactivity disorder; ASD = autism spectrum disorder; CD = conduct disorder; ICD = *International Classification of Diseases*; OCD = obsessive-compulsive disorder; ODD = oppositional defiant disorder; PNES = psychogenic nonepileptic seizures; PTSD = posttraumatic stress disorder.

registrations were obtained from the Danish Data Protection Agency (2016-164), the Danish Health Data Authority (FSEID 00002709), and the Danish Health Authority (3-3013-1859), all of which all approved the study and data use. According to Danish law, patient consents are not required for registry-based studies.

Data Availability

All data used in the study can be obtained by applying to Statistics Denmark.

Results

A total of 384 children and adolescents with PNES were included in this study (female proportion 81.8%, median age at inclusion 15.7 years [interquartile range 14.1–16.8 years]). Coexisting epileptic seizures were present in 54 (14.1%) of the children and adolescents with PNES. The 2 matched control groups consisted of 1,152 children and adolescents with ES and 1,920 HC. As outlined in table 2, the cases of PNES had the highest psychiatric service use both before the index date and within the 2-year follow-up. Furthermore, the cases of PNES had the highest prevalence of parental psychiatric history. The spectrum of parental psychiatric disorders for each group is outlined in table 3.

Risk of Psychiatric Disorders

Among the children and adolescents with PNES, 153 (39.8%) had a prevalent psychiatric disorder at index, and 150 (39.1%) received an incident psychiatric disorder diagnosis in the 2 years after index.

An elevated risk of any psychiatric disorder was observed in the cases of PNES for both prevalent and incident diagnoses compared to the ES group (prevalent: adjusted $RR_{PNES/ES}$ 1.87, 95% CI 1.59–2.21; incident: adjusted $RR_{PNES/ES}$ 2.33, 95% CI 1.92–2.83) and the HC group (prevalent: adjusted $RR_{PNES/HC}$ 5.54, 95% CI 4.50–6.81; incident: adjusted $RR_{PNES/HC}$ 8.37, 95% CI 6.31–11.11) (tables 4 and 5).

Table 2 Characteristics of 384 Children and Adolescents With PNES and Their Matched Controls With ES and HC[a]

	PNES (n = 384), n (%)	ES (n = 1,152), n (%)	HC (n = 1,920), n (%)
Age at inclusion, median (IQR), y	15.7 (14.1–16.8)	15.7 (14.1–16.8)	15.7 (14.1–16.8)
Female sex	314 (81.8)	942 (81.8)	1,570 (81.8)
Psychiatric service use before the index date	90 (23.4)	195 (16.9)	112 (5.8)
Psychiatric service use within 2 y after index date	148 (38.5)	174 (15.1)	72 (3.8)
Parental history of psychiatric disorders	141 (18.5)	358 (15.8)	446 (11.8)
Parents' highest level of education at index date[a]			
Primary	54 (14.1)	159 (13.8)	187 (9.7)
Secondary	9 (2.3)	31 (2.7)	54 (2.8)
Vocational	163 (42.5)	494 (42.9)	791 (41.2)
College	155 (40.4)	458 (39.8)	875 (45.6)
Unknown	3 (0.8)	10 (0.9)	13 (0.7)

Abbreviations: ES = epilepsy; HC = healthy controls; IQR = interquartile range; PNES = psychogenic nonepileptic seizures.
[a] Parental educational information was missing for <1% of the parents in the PNES, ES, and HC population.

Spectrum of Psychiatric Disorders

In the cases of PNES, the prevalent psychiatric disorders consisted most frequently of adjustment disorders (17.5%), SSRD (12.5%), neurodevelopmental disorders (11.5%), emotional disorders (10.7%), and intellectual disabilities (6.8%) (table 4). The most frequent incident disorders in the cases of PNES were adjustment disorders (12.5%), emotional disorders (9.9%), somatic symptom disorders (9.1%), and psychotic disorders (7.4%), followed by neurodevelopmental disorders (6.5%) (table 5). In a comparison of the cases of PNES and the ES group, the highest RRs were observed for prevalent SSRD (adjusted $RR_{PNES/ES}$ 9.40, 95% CI 5.31–16.64), personality disorders (adjusted $RR_{PNES/ES}$ 2.94, 95% CI 1.17–7.36), and adjustment disorders (adjusted $RR_{PNES/ES}$ 2.14, 95% CI 1.60–2.86) (table 4). The risk of all incident psychiatric disorders reported was higher in the PNES group compared to the ES group (table 5). Comparing the PNES group to the HC showed that higher risks were observed for all prevalent and incident psychiatric disorders (tables 4 and 5).

Table 3 Parental History of Psychiatric Disorders in the PNES Study Population and Their Matched Control Groups[a]

	PNES (n = 761), n (%)	ES (n = 2,268), n (%)	HC (n = 3,789), n (%)
Emotional disorders	48 (6.3)	144 (6.4)	194 (5.1)
Adjustment disorders	52 (6.8)	146 (6.4)	173 (4.6)
Neurodevelopmental disorders	16 (2.1)	25 (1.1)	26 (0.7)
Intellectual disabilities	0 (0.0)	4 (0.2)	6 (0.2)
SSRD	5 (0.7)	25 (1.1)	32 (0.8)
Personality disorders	25 (3.3)	71 (3.1)	54 (1.4)
Psychotic disorders	8 (1.1)	28 (1.2)	28 (0.7)
Eating disorders	<4 (<0.5)	7 (0.3)	13 (0.3)
Self-harm	9 (1.2)	27 (1.2)	25 (0.7)
Substance use	61 (8.0)	140 (6.2)	136 (3.6)
≥2 Psychiatric disorders	54 (7.1)	154 (6.8)	160 (4.2)

Abbreviations: ES = epilepsy; HC = healthy controls; PNES = psychogenic nonepileptic seizures; SSRD = somatic symptom and related disorders.
[a] Information on parental history of psychiatric disorders was missing in the following number of children and adolescents from the study populations: PNES n = 7 (1.8%); ES controls n = 34 (3.0%), HC n = 46 (2.4%).

Table 4 Prevalent Psychiatric Disorders in 384 Children and Adolescents With PNES 5 to 17 Years of Age and Their Matched Controls With ES and HC[a]

	PNES (n = 384)	ES (n = 1,152)	HC (n = 1,920)	*p* Value (Wald)
Emotional disorders, n (%)	41 (10.7)	74 (6.4)	39 (2.0)	
Crude RR		1.66 (1.16–2.39)	5.26 (3.44–8.04)	<0.0001
Adjusted RR		1.65 (1.15–2.38)	5.20 (3.40–7.98)	<0.0001
Adjustment disorders, n (%)	67 (17.5)	93 (8.1)	37 (1.9)	
Crude RR		2.16 (1.61–2.89)	9.05 (6.15–13.32)	<0.0001
Adjusted RR		2.14 (1.60–2.86)	8.50 (5.75–12.56)	<0.0001
Neurodevelopmental disorders, n (%)	44 (11.5)	97 (8.4)	52 (2.7)	
Crude RR		1.36 (0.97–1.91)	4.23 (2.88–6.23)	<0.0001
Adjusted RR		1.37 (0.98–1.92)	3.92 (2.67–5.76)	<0.0001
Intellectual disabilities, n (%)	26 (6.8)	70 (6.1)	27 (1.4)	
Crude RR		1.11 (0.72–1.72)	4.81 (2.84–8.16)	<0.0001
Adjusted RR		1.12 (0.72–1.73)	4.50 (2.64–7.66)	<0.0001
SSRD, n (%)	48 (12.5)	15 (1.3)	<4 (<0.2)	
Crude RR		9.60 (5.44–16.95)	—	—
Adjusted RR		9.40 (5.31–16.64)	—	—
Personality disorders, n (%)	9 (2.3)	9 (0.8)	4 (0.2)	
Crude RR		3.00 (1.20–7.50)	—	—
Adjusted RR		2.94 (1.17–7.36)	—	—
Psychotic disorders, n (%)	11 (2.9)	34 (3.0)	<4 (<0.2)	
Crude RR		0.97 (0.50–1.90)	—	—
Adjusted RR		0.98 (0.50–1.92)	—	—
Eating disorders, n (%)	<4 (<1.0)	15 (1.3)	12 (0.6)	
Crude RR		—	—	—
Adjusted RR		—	—	—
Self-harm, n (%)	4 (1.0)	13 (1.1)	<4 (<0.2)	
Crude RR		—	—	—
Adjusted RR		—	—	—
Substance use, n (%)	7 (1.8)	30 (2.6)	18 (0.9)	
Crude RR		0.70 (0.31–1.58)	1.94 (0.82–4.62)	0.003
Adjusted RR		0.70 (0.31–1.56)	1.87 (0.79–4.43)	0.004
≥2 Disorders, n (%)	63 (16.4)	124 (10.8)	44 (2.3)	
Crude RR		1.52 (1.15–2.02)	7.16 (4.95–10.36)	<0.0001
Adjusted RR		1.50 (1.14–1.99)	6.70 (4.62–9.70)	<0.0001
Any psychiatric disorder, n (%)	153 (39.8)	245 (21.3)	132 (6.9)	
Crude RR		1.87 (1.59–2.21)	5.80 (4.72–7.12)	<0.0001
Adjusted RR		1.87 (1.59–2.21)	5.54 (4.50–6.81)	<0.0001

Abbreviations: ES = epilepsy; HC = healthy controls; PNES = psychogenic nonepileptic seizures; RR = relative risk; SSRD = somatic symptom and related disorders.
Adjusted for parental history of psychiatric disorders and parents' highest level of education.
[a] RRs are presented with corresponding 95% confidence intervals (CIs) and reported as inverse for a more intuitive interpretation. Each individual can be represented in >1 of the diagnostic categories. Due to data protection rules in Denmark, observations >0 but <4 were set as <4, and RRs, corresponding CIs, and *p* values based on observations <5 were set as —.

Table 5 Incident Psychiatric Disorders in 384 Children and Adolescents With PNES 5 to 17 Years of Age and Their Matched Control Groups With ES and HC[a]

	PNES (n = 384)	ES (n = 1,152)	HC (n = 1,920)	*p* Value (Wald)
Emotional disorders, n (%)	38 (9.9)	41 (3.7)	15 (0.8)	
Crude RR		2.78 (1.82–4.26)	12.67 (7.04–22.80)	<0.0001
Adjusted RR		2.88 (1.85–4.48)	12.95 (6.80–24.64)	<0.0001
Adjustment disorders, n (%)	48 (12.5)	60 (5.2)	24 (1.3%)	
Crude RR		2.40 (1.67–3.45)	10.00 (6.20–16.12)	<0.0001
Adjusted RR		2.26 (1.55–3.30)	9.05 (5.30–15.45)	<0.0001
Neurodevelopmental disorders, n (%)	25 (6.5)	30 (2.6)	15 (0.8)	
Crude RR		2.50 (1.49–4.20)	8.33 (4.43–15.66)	<0.0001
Adjusted RR		2.57 (1.47–4.48)	8.64 (4.21–17.74)	<0.0001
Intellectual disabilities, n (%)	17 (4.4)	19 (1.7)	5 (0.3)	
Crude RR		2.68 (1.41–5.11)	17.00 (6.31–45.81)	<0.0001
Adjusted RR		2.61 (1.30–5.26)	14.14 (4.63–43.15)	<0.0001
SSRD, n (%)	35 (9.1)	29 (2.5)	<4 (<0.2)	
Crude RR		3.62 (2.24–5.84)	—	—
Adjusted RR		3.31 (1.99–5.51)	—	—
Personality disorders, n (%)	19 (5.0)	17 (1.5)	6 (0.3)	
Crude RR		3.35 (1.76–6.39)	15.83 (6.36–39.39)	<0.0001
Adjusted RR		2.23 (1.17–4.27)	6.59 (2.36–18.39)	<0.0001
Psychotic disorders, n (%)	28 (7.3)	24 (2.1)	4 (0.2)	
Crude RR		3.50 (2.05–5.96)	—	—
Adjusted RR		2.70 (1.53–4.76)	—	—
Eating disorders, n (%)	10 (2.6)	10 (0.9)	5 (0.3)	
Crude RR		3.00 (1.26–7.15)	10.00 (3.44–29.10)	<0.0001
Adjusted RR		2.72 (1.08–6.85)	8.09 (2.48–26.44)	0.0001
Self-harm, n (%)	<4 (<1.0)	10 (0.9)	4 (0.2)	
Crude RR		—	—	—
Adjusted RR		—	—	—
Substance use, n (%)	19 (5.0)	27 (2.3)	18 (0.9)	
Crude RR		2.11 (1.19–3.75)	5.28 (2.80–9.96)	<0.0001
Adjusted RR		1.84 (1.03–3.27)	3.91 (1.98–7.73)	<0.0001
≥2 Disorders, n (%)	53 (13.8)	63 (5.5)	21 (1.1)	
Crude RR		2.52 (1.78–3.57)	12.62 (7.70–20.67)	<0.0001
Adjusted RR		2.23 (1.54–3.24)	10.03 (5.72–17.58)	<0.0001
Any psychiatric disorder, n (%)	150 (39.1)	174 (15.1)	72 (3.8)	
Crude RR		2.59 (2.15–3.11)	10.42 (8.04–13.49)	<0.0001
Adjusted RR		2.33 (1.92–2.83)	8.37 (6.31–11.11)	<0.0001

Abbreviations: ES = epilepsy; HC = healthy controls; PNES = psychogenic nonepileptic seizures; RR = relative risk. SSRD = somatic symptom and related disorders.
Adjusted for any prevalent psychiatric disorder, parental history of psychiatric disorders, and parents' highest level of education.
[a] RRs are presented with corresponding 95% confidence intervals (CIs) and reported as inverse for a more intuitive interpretation. Each individual can be represented in >1 of the diagnostic categories. Due to data protection rules in Denmark, observations >0 but <4 were set as <4, and RRs, corresponding CIs, and *p* values based on observations <5 were set as —.

Subtypes of Psychiatric Disorders

Figures 1 and 2 illustrate the distribution of subtypes of emotional disorders and neurodevelopmental disorders in the cases of PNES and the control groups, respectively. Anxiety disorders and mood disorders were most common in the cases of PNES when we investigated the emotional disorders category, with anxiety disorders being the most prominent of the incident disorders in the cases of PNES (figure 1). Among the neurodevelopmental disorders, ADHD/ADD was the most common prevalent and incident disorder in the cases of PNES (figure 2).

Sensitivity and Stratified Analyses

The analyses stratified on sex, age, and the coexistence of epileptic seizures showed similar occurrence and distribution of psychiatric disorders among all subgroups in the PNES population, and the calculated RRs remained comparable as well (data not shown). Furthermore, a post hoc stratified analyses was conducted regarding the incident psychiatric disorders in which children and adolescents with PNES having coexisting prevalent diagnoses of intellectual disabilities or neurodevelopmental disorders were compared to the group of children and adolescents with PNES having other prevalent psychiatric diagnoses. The risk of any incident psychiatric diagnosis was comparable for the 2 groups.

The sensitivity analyses conducted on subpopulations included cases of PNES with the following characteristics: (1) no coexisting ES (n = 330), (2) a video EEG–confirmed PNES diagnosis (n = 89), and (3) age >12 years at index (n = 346). All sensitivity analyses were robust to the study findings showing comparable results regarding the observed occurrence of psychiatric disorders and the calculated RRs for both the prevalent and incident psychiatric disorders (data not shown).

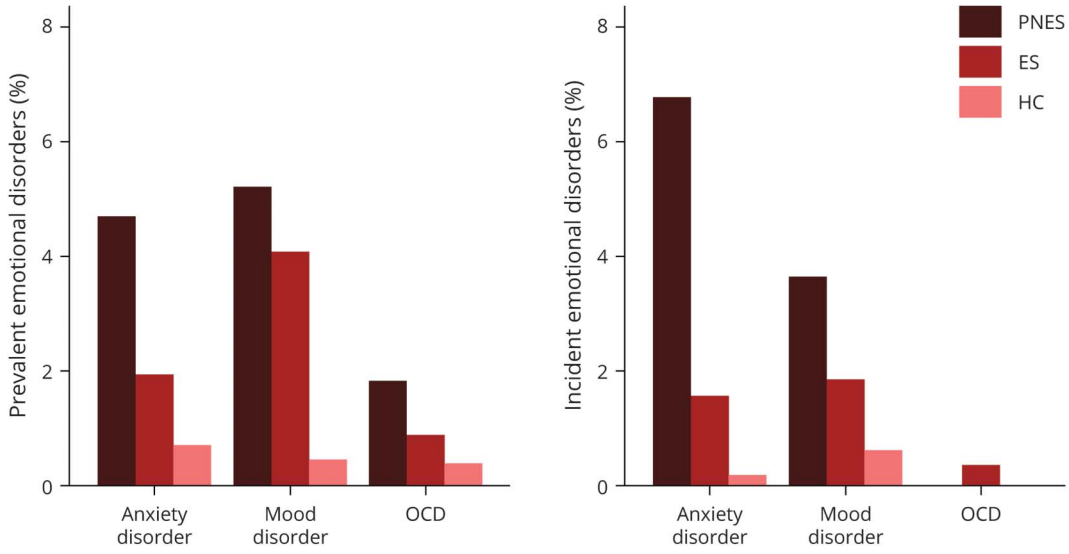
The distribution of time of first incident psychiatric diagnosis with respect to index (0–24 months after) was heavily left-skewed in the ES population and even more so in the PNES population, while it was uniform for the HC. More specifically, >40% of the PNES population and ≈25% of the ES controls received their first incident psychiatric diagnosis in the 2 months after the index date, as opposed to the HC, of whom ≈4% of incident psychiatric diagnoses were given each month in the period of 0 to 24 months after the index date (data not shown).

Discussion

This nationwide matched cohort study found that children and adolescents with PNES have an increased risk of psychiatric disorders both at the time of PNES diagnosis and in the following 2 years compared to matched children and adolescents with ES and matched children and adolescents without PNES or ES. Furthermore, the study shows that PNES in children and adolescents is associated with a wide spectrum of psychiatric disorders.

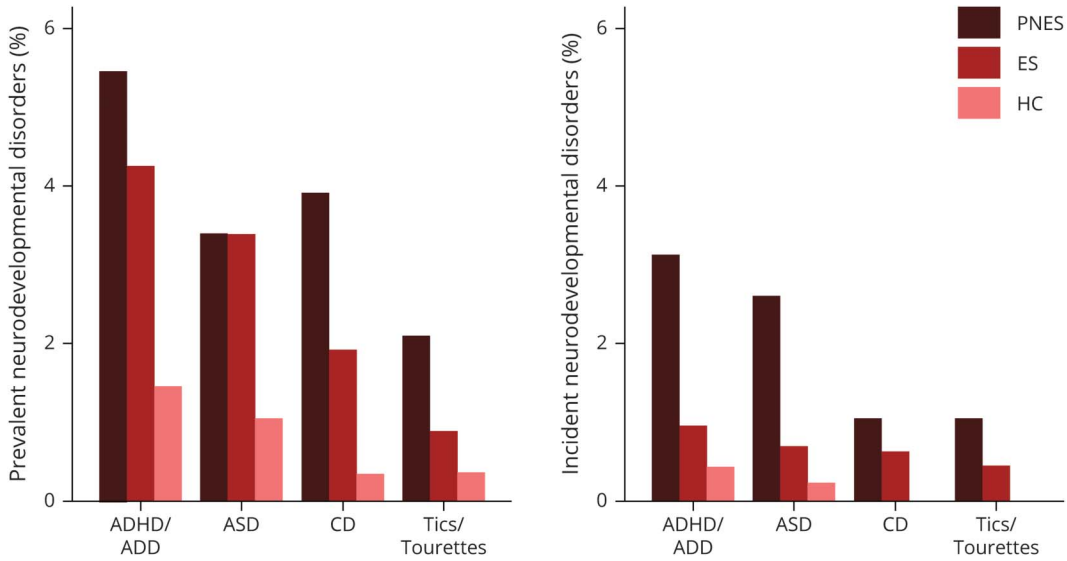
Previous knowledge of a possible association between PNES and psychiatric disorders in children and adolescents is expanded with the results presented in this study. In our study, 39.8% had a prevalent psychiatric disorder and 39.1% received an incident psychiatric diagnosis in the first 2 years after their PNES diagnosis. In smaller study populations, the occurrence of comorbid psychiatric disorders has generally been reported

Figure 1 Prevalent and Incident Emotional Disorder Subgroups in the PNES, ES, and HC Populations



Each individual can be represented in >1 of the diagnostic subgroups. Due to data protection rules in Denmark, observations <3 were not reported. ES = epilepsy; HC = healthy controls; OCD = obsessive compulsive disorder; PNES = psychogenic nonepileptic seizures.

Figure 2 Prevalent and Incident Neurodevelopmental Disorder Subgroups in the PNES, ES, and HC Populations



Each individual can be represented in >1 of the diagnostic subgroups. Due to data protection rules in Denmark, observations <3 were not reported. ADHD = attention-deficit/hyperactivity disorder; ADD = attention-deficit disorder; ASD = autism spectrum disorder; CD = conduct disorder; ES = epilepsy; HC = healthy controls; PNES = psychogenic nonepileptic seizures.

at higher frequencies than found in our study.[1,3,13] This could be due to the fact that most previous studies have been conducted on highly selected populations recruited from specialized tertiary treatment units likely consisting of cases of more complex PNES with higher levels of psychiatric comorbidity. The current study uses a unique nationwide population-based cohort, resulting in less selection and a higher degree of generalizability to all children and adolescents diagnosed with PNES.

In previous studies of children and adolescents with PNES, emotional disorders, i.e., depression (range 2.5%–63%),[23,24] anxiety disorders (range 12%–83%),[6,25] and adjustment disorders primarily in the form of posttraumatic stress disorder (range 2.7%–25.5%),[6,26] have been reported most frequently. Emotional disorders and adjustment disorders were also found to be frequent in our study, and as seen in prior studies,[6,15] anxiety disorders were most prominent among the emotional disorders. However, in addition to existing studies, SSRD and neurodevelopmental disorders were frequent in our study. Few prior studies have investigated SSRD in children and adolescents with PNES,[14,15,27] whereas PNES is commonly reported as associated with other dissociative and somatoform disorders in adults.[21] Still, 2 prior studies have shown more somatic awareness and higher scores regarding the occurrence of unspecific somatic symptoms compared to both siblings and children and adolescents with ES.[6,28] In the context of our results, this underscores the importance of a thorough screening for SSRDs in children and adolescents with PNES and is in line with the recommended management of functional neurologic symptoms in the adult population.[29]

Neurodevelopmental disorders were observed in a substantial proportion of our cases of PNES compared to the ES and HC groups. Previous data based on small study samples have indicated even higher frequencies of ADHD than found in our results, with numbers as high as 29.1%.[6] Still, ADHD represented the main proportion of neurodevelopmental disorders in our cases of PNES. Regarding ASD, we observed an occurrence in the cases of PNES comparable to that found in the ES group. To the best of our knowledge, only 1 prior study has described the occurrence of autism in childhood-onset PNES, reporting a prevalence of 16.9%,[11] thus at a substantially higher occurrence compared to our cases of PNES. This could, as for ADHD, be due to a more representative sample and less selection bias in our study, but differences in the female proportion of the PNES study samples could also affect the prevalence observed. Our study had a female proportion of 81.8%, whereas the study by McWilliams et al.[11] had a female proportion of 62.7%. Neurodevelopmental disorders are more common among boys than among girls in the general population,[30] and differences in the occurrence of psychiatric disorders among boys and girls are important to acknowledge in the interpretation of our results. Still, our results showed a similar occurrence of psychiatric disorders among boys and girls, indicating that PNES is associated with psychiatric disorders regardless of sex.

In this study, neurodevelopmental disorders were less frequent in cases of PNES after the diagnosis of PNES, while psychotic disorders became more frequent. This could be due to the general developmental progress of psychiatric disorders seen in children and adolescents; our PNES population had a median age at index of 15.7 years, with neurodevelopmental

disorders most often being diagnosed during early childhood, whereas psychotic disorders more commonly present in adolescence or early adulthood.[30]

Overall, a bidirectional relationship between PNES and psychiatric disorders is suggested by our results and could be due to shared etiologic factors for PNES and psychiatric disorders. A multifactorial approach to PNES has been outlined that integrates biological, psychological, and socioenvironmental risk factors, with comorbid psychiatric disorders being proposed as a true comorbidity, a predisposition, or an underlying cause.[21] Psychosocial factors and psychiatric disorders are often mentioned as closely linked to PNES, but biological factors may also play an important role in our understanding of PNES.[31] Neuroimaging studies have suggested brain circuit malfunctioning as an explanation for the neurologic symptoms of PNES due to a link between emotional regulation and neurobiological processes,[32,33] and the emotional dysregulation may again explain the link between PNES and various psychiatric disorders.[34] As a result, a multifactorial biopsychosocial approach is recommended when managing children and adolescents with PNES.

The strengths of this study include the use of population-based nationwide data spanning 2 decades. Every Danish citizen is covered by free public health care, and the register-based health care data allow nationwide coverage of all hospital contacts as inpatients or outpatients with a minimal loss to follow-up, therefore reducing bias arising from sampling and attrition. Thus, the registry data made it possible to quantify the occurrence of psychiatric disorders in a population of children and adolescents with PNES included across hospital settings, reducing the risk of selection bias compared to previous studies of highly selected complex cases from tertiary treatment units. In addition, the nationwide registries enabled well-defined matched comparison groups of children and adolescents with ES and HC.

Still, this study has important limitations. As mentioned, most prior studies included cases from specialized tertiary treatment units based on ictal video EEG–validated PNES diagnoses. We chose less narrow criteria with a primary focus on clinical characteristics and witnessed semiology when validating the PNES diagnosis.[20] The included cases in our PNES study sample were nevertheless validated, showing high positive predictive values (PPVs) of the 2 inclusion diagnoses.[20] Likewise, the PPV of the ES register diagnoses has been reported as fairly high.[35] Regarding the psychiatric diagnoses, a proportion of the prevalent psychiatric diagnoses were registered in context of somatic hospital service use, thus also bringing into question the validity, whereas almost all incident psychiatric diagnoses were registered in a psychiatric hospital setting. The validity of the included psychiatric ICD-10 diagnoses has been investigated for some of the diagnoses, showing varying PPVs,[36-40] but the majority of the included psychiatric diagnoses have not been validated in a pediatric population. Still, children and adolescents registered with a psychiatric hospital contact and a psychiatric diagnosis have been referred and are treated in a psychiatric setting due to signs and symptoms resulting in a psychiatric diagnosis and warranting psychiatric hospital-based care. Some level of misclassification is likely present in the included data on psychiatric diagnoses, but the numbers are expected to reflect a degree of psychopathology too severe to be treated in primary care, thus demonstrating the presence of moderate to severe mental health problems in the study populations. Finally, children and adolescents in Denmark can receive treatment for mild mental health problems by both private and public psychology services; however, these cases are not registered in the national registers. Thus, a number of mild cases treated in primary care are not included in our study, resulting in a conservative but uncertain bias regarding the rates of mild psychiatric disorders in the study populations.

Regarding the incident psychiatric diagnoses, some degree of detection bias may exist in the PNES and ES populations. These populations had a higher occurrence of cases receiving their first incident psychiatric diagnosis in the months immediately after the index date compared to the HC. This may indicate that psychiatric disorders are more likely to be recognized in the PNES and ES populations as a consequence of being hospitalized due to the epileptic and nonepileptic seizures. However, we still expect HC with signs and symptoms of moderate to severe mental health disorders to be referred to psychiatric hospital–based care and thereby receive a register diagnosis. The detection bias may therefore concern primarily the mild cases of psychiatric diagnoses. However, we are unable to elucidate such a possible detection bias further within the present study design.

The study included comparison groups, and matching was used to avoid possible confounding introduced by differences in sex and age distribution and year of inclusion in the 3 study populations and to increase the internal validity of the findings. It should be noted that the children and adolescents with ES and the HC represent highly selected study samples due to matching on sex and age, and it is important not to generalize the numbers reported in this study to all cases of ES or children and adolescents from the general population. We did not exclude children and adolescents on the basis of their degree of intellectual disabilities, and we did not include this in our matching criteria. However, we wished the analyses to reflect the broad spectrum of cases found in the general population, including the variation in comorbidity from intellectual disability. Higher rates of severe intellectual disabilities may exist in children and adolescents with ES, and this may be associated with higher rates of psychiatric morbidity. Still, our results showed that children and adolescents with PNES have a higher risk of psychiatric comorbidity than children and adolescents with ES.

Children and adolescents with PNES are at a higher risk of psychiatric disorders both before and in the 2 years after their PNES diagnosis compared to matched children and

adolescents with ES and HC. This study provides evidence that childhood-onset PNES is associated with a wide spectrum of psychiatric disorders, underscoring the need for a careful psychiatric assessment to optimize and individualize the treatment plan. The high risk of psychiatric disorders after the PNES diagnosis indicates a need for systematic follow-up with a repeated psychiatric assessment to ensure continued suitability of the provided treatment.

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Appendix Authors

Name	Location	Contribution
Anne Sofie Hansen, MD	Aalborg University Hospital, Psychiatry, Denmark; Aalborg University, Denmark	Concept and design of the study, acquisition, analysis and interpretation of data, and drafting and revision of the manuscript
Charlotte Ulrikka Rask, MD, PhD	Aarhus University Hospital, Child and Adolescent Psychiatry, Denmark; Aarhus University, Denmark	Concept and design of the study, interpretation of data, and drafting and revision of the manuscript
Ann-Eva Christensen, PhD	Aalborg University Hospital, Psychiatry, Denmark	Concept and design of the study, analysis and interpretation of data, and drafting and revision of the manuscript
Maria Rodrigo-Domingo, PhD	Aalborg University Hospital, Psychiatry, Denmark	Concept and design of the study, analysis and interpretation of data, and drafting and revision of the manuscript
Jakob Christensen, MD, PhD, DrMedSci	Aarhus University Hospital, Aarhus University, Denmark	Concept and design of the study, interpretation of data, and drafting and revision of the manuscript
René Ernst Nielsen, MD, PhD	Aalborg University Hospital, Psychiatry, Denmark. Aalborg University, Denmark	Concept and design of the study, interpretation of data, and drafting and revision of the manuscript

References

1. Doss JL, Plioplys S. Pediatric psychogenic nonepileptic seizures: a concise review. *Child Adolesc Psychiatr Clin N Am.* 2018;27(1):53-61.
2. Reilly C, Menlove L, Fenton V, Das KB. Psychogenic nonepileptic seizures in children: a review. *Epilepsia.* 2013;54(10):1715-1724.
3. Valente KD, Alessi R, Vincentiis S, Dos Santos B, Rzezak P. Risk factors for diagnostic delay in psychogenic nonepileptic seizures among children and adolescents. *Pediatr Neurol.* 2017;67:71-77.
4. McWilliams A, Reilly C, McFarlane FA, Booker E, Heyman I. Nonepileptic seizures in the pediatric population: a qualitative study of patient and family experiences. *Epilepsy Behav.* 2016;59:128-136.
5. Nielsen ES, Wichaidit BT, Ostergaard JR, Rask CU. Paediatricians' attitudes to and management of functional seizures in children. *Eur J Paediatr Neurol.* 2018;22(5):774-781.
6. Plioplys S, Doss J, Siddarth P, et al. A multisite controlled study of risk factors in pediatric psychogenic nonepileptic seizures. *Epilepsia.* 2014;55(11):1739-1747.
7. Heyman I, Reilly C. Seize the opportunity: recognition and management of functional seizures in children. *Eur J Paediatr Neurol.* 2018;22(5):734-735.
8. Goldstein LH, Robinson EJ, Mellers JDC, et al. Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial. *Lancet Psychiatry.* 2020;7(6):491-505.
9. Heyman I. Mind the gap: integrating physical and mental healthcare for children with functional symptoms. *Arch Dis Child.* 2019;104(12):1127-1128.
10. Tolchin B, Dworetzky BA, Martino S, Blumenfeld H, Hirsch LJ, Baslet G. Adherence with psychotherapy and treatment outcomes for psychogenic nonepileptic seizures. *Neurology.* 2019;92(7):e675-e679.
11. McWilliams A, Reilly C, Gupta J, Hadji-Michael M, Srinivasan R, Heyman I. Autism spectrum disorder in children and young people with non-epileptic seizures. *Seizure.* 2019;73:51-55.
12. Luthy SK, Moss AF, Torok MR, McLeod L, Wilson KM. Characteristics of children hospitalized for psychogenic nonepileptic seizures due to conversion disorder versus epilepsy. *Hosp Pediatr.* 2018;8(6):321-329.
13. Myers L, Trobliger R, Bortnik K, Zeng R, Segal E, Lancman M. Dissociation and other clinical phenomena in youth with psychogenic non-epileptic seizures (PNES) compared to youth with epilepsy. *Seizure.* 2019;70:49-55.
14. Kozlowska K, Chudleigh C, Cruz C, et al. Psychogenic non-epileptic seizures in children and adolescents, part I: diagnostic formulations. *Clin Child Psychol Psychiatry.* 2018;23(1):140-159.
15. Sawchuk T, Buchhalter J, Senft B. Psychogenic nonepileptic seizures in children: prospective validation of a clinical care pathway & risk factors for treatment outcome. *Epilepsy Behav.* 2020;105:106971.
16. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol.* 2015;7:449-490.
17. Mors O, Perto GP, Mortensen PB. The Danish Psychiatric Central Research Register. *Scand J Public Health.* 2011;39(7 suppl):54-57.
18. Jensen VM, Rasmussen AW. Danish education registers. *Scand J Public Health.* 2011;39(7 suppl):91-94.
19. LaFrance WCJ, Baker GA, Duncan R, Goldstein LH, Reuber M. Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: a staged approach: a report from the International League Against Epilepsy Nonepileptic Seizures Task Force. *Epilepsia.* 2013;54(11):2005-2018.
20. Hansen AS, Rask CU, Rodrigo-Domingo M, Pristed SG, Christensen J, Nielsen RE. Incidence rates and characteristics of pediatric onset psychogenic nonepileptic seizures. *Pediatr Res.* 2020;88(5):796-803.
21. Popkirov S, Asadi-Pooya AA, Duncan R, et al. The aetiology of psychogenic non-epileptic seizures: risk factors and comorbidities. *Epileptic Disord.* 2019;21(6):529-547.
22. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol.* 2004;159(7):702-706.

23. Madaan P, Gulati S, Chakrabarty B, et al. Clinical spectrum of psychogenic non epileptic seizures in children; an observational study. *Seizure*. 2018;59():60-66.
24. Pakalnis A, Paolicchi J. Frequency of secondary conversion symptoms in children with psychogenic nonepileptic seizures. *Epilepsy Behav.* 2003;4(6):753-756.
25. Yi YY, Kim HD, Lee JS, Cheon K-A, Kang H-C. Psychological problems and clinical outcomes of children with psychogenic non-epileptic seizures. *Yonsei Med J.* 2014;55(6):1556-1561.
26. Verrotti A, Agostinelli S, Mohn A, et al. Clinical features of psychogenic non-epileptic seizures in prepubertal and pubertal patients with idiopathic epilepsy. *Neurol Sci.* 2009;30(4):319-323.
27. Akdemir D, Uzun O, Pehlivanturk Ozsungur B, Topcu M. Health-related quality of life in adolescents with psychogenic nonepileptic seizures. *Epilepsy Behav.* 2013;29(3):516-520.
28. Salpekar JA, Plioplys S, Siddarth P, et al. Pediatric psychogenic nonepileptic seizures: a study of assessment tools. *Epilepsy Behav.* 2010;17(1):50-55.
29. Stone J. Functional neurological symptoms. *Clin Med J R Coll Physicians Lond.* 2013;13(1):80-83.
30. Steinhausen HC, Jakobsen H. Incidence rates of treated mental disorders in childhood and adolescence in a complete nationwide birth cohort. *J Clin Psychiatry.* 2019;80(3):17m12012.
31. Barzegaran E, Carmeli C, Rossetti AO, Frackowiak RS, Knyazeva MG. Weakened functional connectivity in patients with psychogenic non-epileptic seizures (PNES) converges on basal ganglia. *J Neurol Neurosurg Psychiatry.* 2016;87(3):332-337.
32. Voon V, Cavanna AE, Coburn K, Sampson S, Reeve A, LaFrance WCJ. Functional neuroanatomy and neurophysiology of functional neurological disorders (conversion disorder). *J Neuropsychiatry Clin Neurosci.* 2016;28(3):168-190.
33. Arthuis M, Micoulaud-Franchi JA, Bartolomei F, McGonigal A, Guedj E. Resting cortical PET metabolic changes in psychogenic non-epileptic seizures (PNES). *J Neurol Neurosurg Psychiatry.* 2015;86(10):1106-1112.
34. Berking M, Wupperman P. Emotion regulation and mental health: recent findings, current challenges, and future directions. *Curr Opin Psychiatry.* 2012;25(2):128-134.
35. Christensen J, Vestergaard M, Olsen J, Sidenius P. Validation of epilepsy diagnoses in the Danish National Hospital Register. *Epilepsy Res.* 2007;75(2-3):162-170.
36. Mohr-Jensen C, Vinkel Koch S, Briciet Lauritsen M, Steinhausen HC. The validity and reliability of the diagnosis of hyperkinetic disorders in the Danish Psychiatric Central Research Registry. *Eur Psychiatry.* 2016;35:16-24.
37. Vernal DL, Stenstrøm AD, Staal N, et al. Validation study of the early onset schizophrenia diagnosis in the Danish Psychiatric Central Research Register. *Eur Child Adolesc Psychiatry.* 2018;27(8):965-975.
38. Nissen J, Powell S, Koch SV, et al. Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample. *BMJ Open.* 2017;7(9):e017172.
39. Lauritsen MB, Jørgensen M, Madsen KM, et al. Validity of childhood autism in the Danish Psychiatric Central Register: findings from a cohort sample born 1990-1999. *J Autism Dev Disord.* 2010;40(2):139-148.
40. Frederiksen LH, Bilenberg N, Andersen L, et al. The validity of child and adolescent depression diagnoses in the Danish Psychiatric Central Research Register. *Acta Psychiatr Scand.* 2021;143(3):264-274.

Psychiatric Disorders in Children and Adolescents With Psychogenic Nonepileptic Seizures

Anne Sofie Hansen, Charlotte Ulrikka Rask, Ann-Eva Christensen, et al.

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