

Childhood Epilepsy, Febrile Seizures, and Subsequent Risk of ADHD

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abstract

OBJECTIVES: Epilepsy, febrile seizures, and attention-deficit/hyperactivity disorder (ADHD) are disorders of the central nervous system and share common risk factors. Our goal was to examine the association in a nationwide cohort study with prospective follow-up and adjustment for selected confounders. We hypothesized that epilepsy and febrile seizures were associated with subsequent ADHD.

METHODS: A population-based cohort of all children born in Denmark from 1990 through 2007 was followed up until 2012. Incidence rate ratios (IRRs) and 95% confidence intervals (95% CIs) for ADHD were estimated by using Cox regression analysis, comparing children with epilepsy and febrile seizure with those without these disorders, adjusted for socioeconomic and perinatal risk factors, as well as family history of neurologic and psychiatric disorders.

RESULTS: A total of 906 379 individuals were followed up for 22 years (~10 million person-years of observation); 21 079 individuals developed ADHD. Children with epilepsy had a fully adjusted IRR of ADHD of 2.72 (95% CI, 2.53–2.91) compared with children without epilepsy. Similarly, in children with febrile seizure, the fully adjusted IRR of ADHD was 1.28 (95% CI, 1.20–1.35). In individuals with both epilepsy and febrile seizure, the fully adjusted IRR of ADHD was 3.22 (95% CI, 2.72–3.83).

CONCLUSIONS: Our findings indicate a strong association between epilepsy in childhood and, to a lesser extent, febrile seizure and subsequent development of ADHD, even after adjusting for socioeconomic and perinatal risk factors, and family history of epilepsy, febrile seizures, or psychiatric disorders.

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DOI: 10.1542/peds.2015-4654

Accepted for publication Apr 29, 2016

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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WHAT'S KNOWN ON THIS SUBJECT: Several studies have demonstrated an association between seizure disorders and attention-deficit/hyperactivity disorder in childhood. Genetic and environmental risk factors influence this association, but former studies on this subject have been limited by retrospective designs and small sample sizes.

WHAT THIS STUDY ADDS: This prospective population-based study found a strong association between childhood epilepsy and febrile seizures and subsequent attention-deficit/hyperactivity disorder, even after adjusting for perinatal and socioeconomic risk factors, as well as family history of neurologic and psychiatric disorders.

To cite: Bertelsen EN, Larsen JT, Petersen L, et al. Childhood Epilepsy, Febrile Seizures, and Subsequent Risk of ADHD. *Pediatrics*. 2016;138(2):e20154654

The population prevalence of epilepsy has been estimated to be 0.5% to 0.9% worldwide, with the highest incidence rate found in very early childhood.¹ Low gestational age, birth weight,² and Apgar score³ are associated with an increased risk of epilepsy and febrile seizures.⁴ These risk factors have also been associated with an increased risk of attention-deficit/hyperactivity disorder (ADHD).^{5,6} Other common risk factors include parental age,^{7,8} family history, and genetic factors;^{9,10} and this scenario has led to a hypothesis of a common pathophysiological link between epilepsy and psychiatric disorders in general, and ADHD in particular.^{11–13}

Febrile seizure is also a common childhood disorder, affecting 2% to 5% of children before 5 years of age.¹⁴ Several studies have found an increased risk of subsequent epilepsy in children diagnosed with febrile seizure.¹⁵ However, apart from epilepsy, only modest neurodevelopmental consequences of febrile seizures have been identified,¹⁶ and, thus far, studies on ADHD in children with febrile seizures have drawn diverse conclusions.^{17,18}

ADHD is associated with increased morbidity, impairment, and mortality in adolescence and young adulthood.^{19–24} Early identification of high-risk groups may improve their outcome. Among patients with epilepsy, comorbid neurodevelopmental disorders are highly prevalent, including ADHD.^{25–28} Comorbidity studies have shown clear links between epilepsy and various neuropsychiatric disorders, including psychosis and autism. Data support the view that epilepsy and some neuropsychiatric conditions share pathogenic neurodevelopmental pathways, and that epilepsy could be included in the spectrum of neurodevelopmental disorders. ADHD has also been described with increased frequency in persons with epilepsy.²⁸

A population-based cohort study from Taiwan²⁷ found a bidirectional relationship between ADHD and epilepsy. The hazard ratio of ADHD in persons with epilepsy was 2.54 (95% confidence interval [CI], 2.02–3.18), whereas the hazard ratio for epilepsy in persons with ADHD was 3.94 (95% CI, 2.58–6.03). However, the analyses in the Taiwanese study were not adjusted for the potential confounding effects of prenatal risk factors, family history of epilepsy or ADHD, or parental socioeconomic factors. Consequently, that study may have overestimated the association.

The present longitudinal, prospective population-based cohort study investigated the association between epilepsy and febrile seizure in childhood and later ADHD. Our analyses were adjusted for the effect of a number of potentially confounding factors, such as perinatal and socioeconomic risk factors, as well as family history of epilepsy, febrile seizure, and psychiatric disorder.

METHODS

Data Sources

A unique 10-digit Personal Identification Number²⁹ is allocated to all live-born children and new residents of Denmark, and it was used as the key identifier to link data across a number of Danish nationwide registers.³⁰ Information on epilepsy and febrile seizure diagnoses was obtained from the Danish National Hospital Register (DNHR).³¹ Data on ADHD diagnoses were obtained from DNHR and the Danish Psychiatric Central Register (DPCR).³² Inpatient contacts were included in DPCR in 1969 and in DNHR in 1977; outpatient data have been included in both registers since 1995. Diagnostic information in DPCR and DNHR was based on the *International Classification of Diseases, Eighth Edition* (ICD-8), from 1977 to 1993 and the *International*

Classification of Diseases, 10th Edition (ICD-10), from 1994 onwards. Information on maternal and paternal age, gestational age, birth weight, and Apgar score at 5 minutes after birth was obtained from The Danish Medical Birth Register.³³ We obtained information on maternal level of education, as well as paternal income at time of birth, from the Integrated Database for Longitudinal Labor Market Research.³⁴ This database contains longitudinal information on labor market affiliation and sociodemographic data for the total population.

Data were merged and anonymized by an independent government agency (Statistics Denmark). In Denmark, all hospital admissions are tax paid and free of charge for patients, and the nationwide registers accessed in this study cover the entire Danish population. The study was approved by the Danish Data Protection Agency and the Danish Health and Medicines Authority. All personal information from the registers is anonymized when used for research purposes, and by Danish law informed consent is not needed for register-based studies.

Study Population

A cohort consisting of all children born in Denmark between January 1, 1990, and December 31, 2007, was identified in the Danish Civil Registration System³⁵ along with their parents and full siblings. Children in the study population entered the study period on the date of their third birthday or January 1, 1995, whichever came last. The cohort was followed up until the onset of ADHD, emigration, death, or December 31, 2012, whichever came first.

Based on clinical diagnoses in DNHR, we identified children with a first diagnosis of epilepsy (ICD-8, 345, except 345.29; ICD-10, G40) or febrile seizure (ICD-8, 780.21; ICD-10, R56.0). Cohort members were

classified with febrile seizures if they had been admitted or had been in outpatient care between the age of 3 months and 5 years, given they had no previous record of epilepsy or infection in the central nervous system (ICD-8, 320–323; ICD-10, G00–G09). Cohort members were classified as having ADHD, based on data from DPCR and DNHR (ICD-8, 308.01; ICD-10, F90.x and F98.8). If diagnoses of both exposure (epilepsy or febrile seizure) and outcome (ADHD) were obtained the same day, persons were categorized as unexposed. We found no effect of time since exposure diagnosis with regard to risk of ADHD (data not shown). Data on diagnoses of ADHD, epilepsy, febrile seizures, and any psychiatric disorders (ICD-8, 290–315; ICD-10, F00–F99) in parents and siblings were obtained from the DPCR and DNHR.

Statistical Analyses

Incidence rate ratios (IRRs) and 95% CIs of ADHD were estimated by using Cox proportional hazards regression for each of the 3 main exposures: (1) febrile seizure; (2) epilepsy; and (3) febrile seizure and epilepsy. These data were compared with those of children without these disorders. All main exposures were treated as time-dependent variables. Stata version 12 (Stata Corp, College Station, TX) was used in all statistical analyses. We performed partially adjusted (model 1) and fully adjusted (model 2) analyses. In model 1, all estimates were controlled for calendar time as a time-dependent variable, for sex by means of separate underlying hazard functions, and for age in the nonparametric part of the Cox model. Calendar years were categorized as 1995–1999, 2000–2004, 2005–2009, and 2010–2012. In model 2, in addition to the adjustments mentioned in model 1, we adjusted for maternal and paternal ages (in 5-year intervals), level of maternal education at time

of birth (categorized as primary school, secondary school, bachelor's degree, and postgraduate degree), level of paternal income at time of birth divided into quintiles for given calendar year, birth weight (<1500, 1500–2500, 2500–3000, 3000–4000, and >4000 g), gestational age (<33, 33–37, 37–42, and >42 weeks), and 5-minute Apgar score (10 vs <10). We controlled for time-dependent variables describing history of epilepsy, febrile seizure, and psychiatric disorders among first-degree relatives. Family history of psychiatric disorders was considered a hierarchical variable categorized as ADHD, any other psychiatric diagnoses, or no history of psychiatric disorders.

In addition, smoothed age- and sex-specific hazard functions were plotted by using the estimated hazard contributions, adjusted for calendar time.

Sensitivity Analyses

Information was obtained from the DNHR on the first cerebral event or congenital malformation on all subjects in our study population. A cerebral event was defined as a diagnosis of head injury (ICD-8, 851–854 and 850.99; ICD-10, S02 [except S02.2–S02.9], S06, S07, S08, T020, and T040), cerebral palsy (ICD-8, 343.99 and 344.99; ICD-10, G80), or neoplasms in the central nervous system (ICD-8, 191, 225, 192.19, 238.19, 238.39; ICD-10, C70–C71, D32–D33). Diagnoses of congenital malformations (ICD-8, 740–759; ICD-10, Q00–Q89) were also obtained. For this analysis, follow-up time was ended at first occurrence of any of these cerebral events or congenital malformations, date of ADHD diagnosis, death, emigration, or December 31, 2012, whichever came first. Information was used to detect the influence of these early cerebral events, as well as congenital malformations, on the association

between febrile seizure and epilepsy and later development of ADHD.

In addition to the first sensitivity analysis, a restriction on the cohort based on information from the National Birth Register was applied. Children with low gestational weight (<2500 g), children born preterm (before gestational week 37), and children with an Apgar score <10 were excluded.

RESULTS

A cohort of 906 379 children (48.7% female subjects) were followed up for a total of 9 919 977 person-years. In 0.81% of all individuals in the total study population ($n = 7386$), data were censored before outcome due to emigration ($n = 5756$ persons), death ($n = 1619$), or loss to follow-up ($n = 11$). Within the cohort, 13 573 (1.5%) individuals were diagnosed with epilepsy, and 33 947 (3.8%) were diagnosed with febrile seizure. The characteristics of the study population are shown in Table 1.

Within the study cohort, 21 079 children (15 602 male subjects [74%]; 5477 female subjects [26%]) were diagnosed with ADHD. In children diagnosed with epilepsy, the incidence rate of ADHD was 752 per 100 000 person-years; in children with febrile seizure, the incidence rate of ADHD was 303 per 100 000 person-years. In comparison, the incidence rate of ADHD in unexposed children was 204 per 100 000 person-years.

Children with epilepsy had a fully adjusted IRR for ADHD of 2.72 (95% CI, 2.53–2.91), compared with children without epilepsy. Children diagnosed with febrile seizures had a fully adjusted IRR for ADHD of 1.28 (95% CI, 1.20–1.35) compared with children without febrile seizure. In children having both febrile seizures and epilepsy, the fully adjusted IRR for ADHD was 3.22 (95% CI, 2.72–3.83), compared with children

TABLE 1 Population Characteristics (*N* = 906 379)

Characteristic	No Epilepsy or Febrile Seizure (<i>n</i> = 858 611)	Febrile Seizure (<i>n</i> = 33 351)	Epilepsy (<i>n</i> = 12 684)	Both Epilepsy and Febrile Seizure (<i>n</i> = 1733)
Female subjects	48.9	44.5	47.7	45.1
Apgar score <10	7.2	7.6	10.8	10.0
Gestational age, wk				
<33	0.8	1.2	1.9	2.5
33–<37	3.7	4.0	5.0	6.1
37–<42	92.2	90.7	90.3	88.4
>42	3.4	3.2	2.8	3.1
Birth weight, g				
<1500	0.4	0.7	1.3	1.6
1500–2500	2.8	4.0	4.7	4.8
2500–3000	10.0	11.3	12.4	14.4
3000–4000	68.5	67.4	64.7	65.4
>4000	18.3	16.7	16.9	13.8
Parental age (maternal/paternal), y				
<20	1.5/0.5	1.8/0.6	2.3/0.6	2.6/0.8
20–24	13.4/6.9	14.8/7.7	17.6/9.5	16.3/8.7
25–29	38.6/29.3	39.4/30.2	38.7/30.7	39.6/33.4
30–34	33.3/36.5	31.5/36.0	29.6/33.9	29.8/33.8
35–39	11.7/18.9	11.0/17.8	10.4/17.2	9.5/15.6
40–44	1.5/5.9	1.4/5.7	1.5/5.8	2.0/5.3
≥45	0.03/2.1	0.05/2.0	0.02/2.3	0.06/2.5
Paternal income at time of birth, quintiles				
0%–20%	19.8	21.3	23.0	23.7
20%–40%	20.0	20.3	21.5	21.5
40%–60%	20.1	19.8	19.5	20.0
60%–80%	20.1	19.6	18.4	19.0
80%–100%	20.1	19.0	17.6	15.9
Maternal education at time of birth				
Primary school	21.6	23.0	30.5	30.6
Secondary school	45.9	46.1	43.9	43.5
Bachelor degree	25.9	24.7	21.1	22.0
Postgraduate degree	6.6	6.3	4.6	3.9
Neurologic diagnosis among first-degree relatives				
No epilepsy or febrile seizure	91.7	80.0	83.8	73.9
Epilepsy or febrile seizure	8.3	20.0	16.2	26.1
Psychiatric diagnosis among first-degree relatives				
No psychiatry	80.1	78.3	72.7	72.5
Any psychiatry, except ADHD	17.4	19.0	23.9	24.4
ADHD	2.5	2.8	3.4	3.1

Data are presented as percentages. Distribution of children born in Denmark in the period 1990 to 2007 and followed up to 2012. Descriptive data on perinatal and socioeconomic factors are presented, as well as family history of psychiatric and neurologic disorders for nonexposed as well as 3 main exposure groups: (1) febrile seizure; (2) epilepsy; and (3) febrile seizure and epilepsy.

without both febrile seizures and epilepsy (Table 2).

Sex-specific analyses revealed the highest incidence rates of ADHD in male subjects compared with female subjects for all exposure categories

and ages (Fig 1). In the male population, age-specific incidence rates of ADHD peaked at 8 to 9 years of age; double peaks at ages 9 and 16 years were observed in the female population.

The relative risk of ADHD in children with epilepsy, compared with children without epilepsy, was higher in female subjects than in male subjects (IRR of 3.01 in girls [95% CI, 2.66–3.42] and IRR of 2.60

TABLE 2 Estimated IRRs for ADHD and 95% CIs of ADHD for Main Exposures (*N* = 906 379)

Exposure	Exposed, <i>N</i> (%)	No. of Exposed Cases With ADHD	Model 1: IRR (95% CI)	Model 2: IRR (95% CI)
Febrile seizures	35 084 (3.8%)	1137	1.38 (1.30–1.47)	1.28 (1.20–1.35)
Epilepsy	14 417 (1.6%)	844	3.29 (3.07–3.53)	2.72 (2.53–2.91)
Both epilepsy and febrile seizure	1733 (0.2%)	132	3.94 (3.32–4.68)	3.22 (2.72–3.83)

Model 1: adjusted for sex, age and calendar time. Model 2: adjusted for sex, age, calendar time, parental age, paternal income, maternal education, birth weight, gestational age and Apgar score, family history of psychiatric disorders, and family history of neurologic disorders among first-degree relatives.

TABLE 3 Estimated IRRs and 95% CIs of ADHD for Main Exposures in Children Without Cerebral Events and Congenital Malformations

Exposure	Exposed, <i>N</i> (%)	No. of Exposed Cases With ADHD	Model 1: IRR (95% CI)	Model 2: IRR (95% CI)
Febrile seizures	31 567 (3.8%)	879	1.38 (1.29–1.48)	1.29 (1.21–1.38)
Epilepsy	10 657 (1.3%)	577	3.59 (3.30–3.90)	3.00 (2.76–3.26)
Both epilepsy and febrile seizure	1263 (0.2%)	103	5.01 (4.13–6.08)	4.04 (3.33–4.91)

Cohort was restricted to diagnoses of head injury, concussion, cerebral palsy, neoplasms or infections in the central nervous system, and cognitive malformations (*N* = 832 815 persons). Model 1: adjusted for sex, age and calendar time. Model 2: adjusted for sex, age, calendar time, parental age, paternal income, maternal education, birth weight, gestational age and Apgar score, family history of psychiatric disorders, and family history of neurologic disorders among first-degree relatives.

TABLE 4 Estimated IRRs and 95% CIs of ADHD for Main Exposures in Children With Normal Birth Weight, Born at Term, and Children With an Apgar Score <10

Exposure	Exposed, <i>N</i> (%)	No. of Exposed Cases With ADHD	Model 1: IRR (95% CI)	Model 2: IRR (95% CI)
Febrile seizures	27 459 (3.7)	718	1.35 (1.25–1.46)	1.27 (1.18–1.37)
Epilepsy	9144 (1.2)	494	3.73 (3.41–4.08)	3.12 (2.85–3.42)
Both epilepsy and febrile seizure	1076 (0.2)	83	4.91 (3.96–6.09)	4.14 (3.33–5.14)

Cohort was restricted to those with Apgar scores of 10, birth weight >2500 g, and gestational age ≥37 weeks, in addition to the restrictions in Table 3 (*N* = 738 054). Model 1: adjusted for sex, age and calendar time. Model 2: adjusted for sex, age, calendar time, parental age, paternal income, maternal education, birth weight, gestational age and Apgar score, family history of psychiatric disorders, and family history of neurologic disorders among first-degree relatives.

in boys [95% CI, 2.39–2.82]; *P* < .05]. In children with febrile seizures, we found no significant sex difference in the risk for ADHD (IRR was 1.37 [95% CI, 1.22–1.55] in girls and 1.24 [95% CI, 1.16–1.34] in boys; *P* > .05) compared with nonexposed children of the same sex.

Sensitivity Analyses

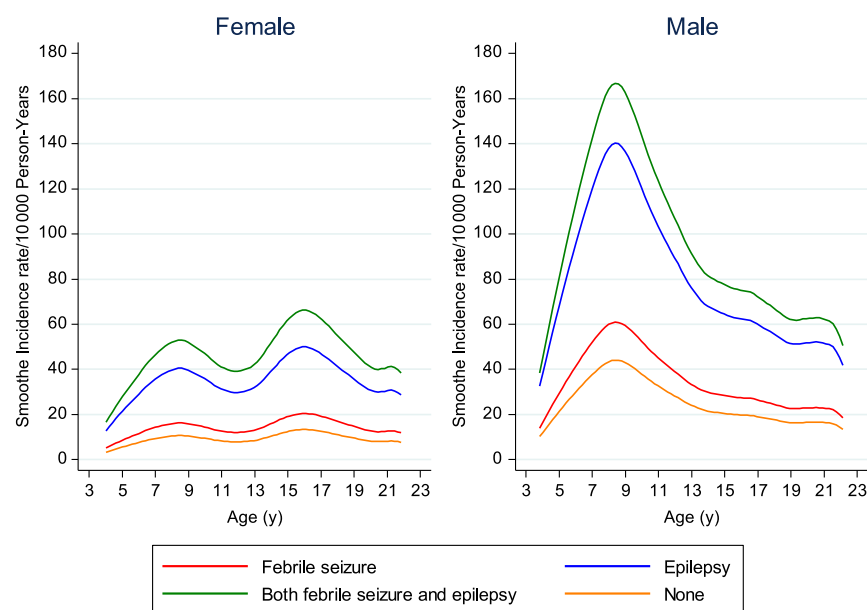
In the first sensitivity analysis, data were censored at the time of occurrence of one of the following cerebral events: head injury (*n* = 5435 persons), cerebral concussion (*n* = 52 226), cerebral palsy (*n* = 3189), cerebral neoplasms (*n* = 781), or infections in the central nervous system (*n* = 3595). Censoring also occurred at diagnoses of congenital malformations (*n* = 94 966). A total of 148 261 individuals were censored either due to a cerebral event or a congenital malformation. Compared with the uncensored analysis, the estimates generally remained unchanged (Table 3).

In addition to the first sensitivity analysis, we restricted the cohort and excluded children with low birth weight (<2500 g, *n* = 24 957), children born preterm (before gestational week 37, *n* = 34 606), and children with an Apgar score <10

(*n* = 57 928). A total of 94 761 children were excluded in this restricted cohort. The association with ADHD in children with febrile seizure remained virtually the same (IRR, 1.27 [95% CI, 1.18–1.37]), whereas in children with epilepsy, a slightly increased risk of ADHD was found (fully adjusted IRR, 3.12 [95% CI, 2.85–3.42]) (Table 4).

DISCUSSION

In this prospective, population-based nationwide cohort study, children diagnosed with epilepsy and/or febrile seizure had a significantly increased incidence rate of subsequent ADHD compared with children without a seizure diagnosis. Children with epilepsy had a 150% to 200% increased risk of ADHD

**FIGURE 1**

Smoothed age- and sex-specific incidence functions according to age of onset at first diagnosis of ADHD, stratified according to exposure type; all Danish individuals born from 1990 to 2007 were included. All analyses were adjusted for calendar year.

compared with children without epilepsy. Children with febrile seizure had a 20% to 35% increased risk of ADHD compared with children without febrile seizures. We also found a tendency toward a dose-dependent-like pattern in the association, as children diagnosed with both febrile seizures and epilepsy had a higher risk of ADHD than children diagnosed with only 1 of the 2 disorders.

Chou et al²⁷ reported a bidirectional association between epilepsy and ADHD in a Taiwanese population, suggesting a common neurologic mechanism in the 2 disorders. However, some methodologic limitations may have biased their results. The study included prevalent cases with epilepsy or ADHD (rather than incident cases), control subjects were not matched at the time of the cases being diagnosed, and no data on deaths were available; all of these factors increased the risk of immortal time bias and an overestimation of the association between epilepsy and ADHD. Although children already diagnosed with ADHD before being included in the study were misclassified as nonexposed, they were more likely to have an additional claim for ADHD later. This bias would mainly affect the oldest age group, and in fact, the study did find the strongest association in individuals with late-onset epilepsy. In addition, substantial residual confounding may be important because estimates were not adjusted for prenatal and perinatal complications, psychiatric or neurologic disorders among family members, or parental socioeconomic status, all of which could influence the association.^{2,3,7,14}

We performed partially and fully adjusted analyses and found confounders influencing the association between childhood epilepsy and febrile seizure and ADHD, but the association cannot

solely be explained by these confounding factors.

Several hypotheses have been suggested for the association between seizures and ADHD. Previous studies of children with ADHD without seizures have found increased rates of pathologic findings on EEG.³⁶ Common environmental risk factors for neurodevelopmental vulnerability predisposing children to both disorders have also been proposed.^{37,38} We did find some common risk factors, but even after adjusting for the effect of these factors, epilepsy was still associated with ADHD. Common genetic risk factors for both disorders could also be an explanation.

Studies on genetic risk factors have suggested a complex heterogeneous pathogenesis involving early brain development and neurohormonal transmission, as well as specific genetic links.^{9,10,39,40} Identification of these genetic links contribute, with high research value, but published findings on this area are based on small and heterogeneous study material. Future studies are required to assess the bidirectional relationship between the genetically based risk factors and environmental influence of comorbid ADHD in patients with epilepsy.

Our study has some limitations. Data in the hospital registers were based on clinical diagnoses, not the results of assessments using systematic psychometric diagnostic instruments. However, validation studies have shown high quality in diagnoses of febrile seizure, epilepsy, and ADHD obtained in these Danish registers. We found that the predictive value of a febrile seizure diagnosis was 93%,⁴¹ the value of an epilepsy diagnosis was 81%,⁴² and the value of an ADHD diagnosis was 84%.⁴³ We did not include data on diagnoses from private practices (only from public hospital departments). However, in Denmark, the majority of individuals with epilepsy and febrile seizures

are referred to a hospital department (typically either departments of pediatrics or neurology) and are rarely assessed in private practices. Some children diagnosed with ADHD are diagnosed in private practice, and these may have been misclassified as non-ADHD cases. Still, such misclassification would only lead to an underestimation of the association between epilepsy and febrile seizures and ADHD.

The included children diagnosed with ADHD at hospital departments may represent those with the most severely impairing symptoms; the generalizability of our results may therefore be affected, and the association most likely reflects an association between epilepsy and febrile seizure and patients with severe symptoms of ADHD. In addition, we had no information on drug prescriptions, and pharmacologic treatment of children with epilepsy may influence the risk of developing symptoms of ADHD.⁴⁴ Children diagnosed with epilepsy going to regular evaluations at a hospital department may have a higher probability of being referred to a specialist for assessment of ADHD, compared with children without epilepsy, and the physician treating the epilepsy may have knowledge regarding the association between epilepsy and ADHD and thus be more likely to refer the child for psychiatric evaluation. This form of Berkson's bias affecting only treatment-seeking patients could lead to a higher rate of ADHD cases in these patients, and thereby an overestimation of the association.⁴⁵ Finally, severity of the convulsions may influence the risk of developing ADHD, as may the nature of febrile seizures (simple versus complex). However, we had no data on this topic. Analysis of subtypes of epilepsy was not performed because of the relatively low number of such subtypes in DNHR and because of insufficient discriminate validity of

subtype diagnoses of epilepsy in the register.⁴² Patients were assigned to the epilepsy group at first onset of epilepsy, regardless of subtype. Furthermore, we did not examine the effect of repeated admissions due to epilepsy or a possible dose–response effect in the association. Hence, whether seizure frequency, severity, or subtype or age of onset, modify the association with ADHD is yet to be studied.

Identifying groups of children at high risk of ADHD is important because having this disorder is known to increase use of health services²² and the risk of injuries,⁴⁶ substance use disorder,^{21,47} criminality,¹⁹ psychotic disorders,^{48,49} and premature death.²³

CONCLUSIONS

We found a higher risk of developing ADHD among individuals with

epilepsy and febrile seizures, even after adjusting for the effect of birth weight, gestational age, Apgar score, family history of epilepsy or neurodevelopmental disorders, parental age, and parental socioeconomic status, including paternal income and maternal level of education. Children with epilepsy had a threefold increased IRR of ADHD compared with those without epilepsy. Similarly, children with febrile seizures had a 30% increased risk of ADHD. Our sensitivity analyses showed that the association was not explained by cerebral traumas, congenital malformations, or by birth complications.

It is important for clinicians to identify early symptoms of ADHD in patients with epilepsy and febrile seizure, to initiate proper assessment and treatment, and thereby reduce the likelihood of negative long-term consequences of ADHD.

ACKNOWLEDGMENTS

The authors thank The Lundbeck Foundation and the collaborative research initiatives *iPSYCH* and CIRRAU for supporting this study.

ABBREVIATIONS

ADHD:	attention-deficit/hyperactivity disorder
CI:	confidence interval
DNHR:	Danish National Hospital Register
DPCR:	Danish Psychiatric Central Register
ICD-8:	<i>International Classification of Diseases, Eighth Edition</i>
ICD-10:	<i>International Classification of Diseases, 10th Edition</i>
IRR:	incidence rate ratio

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by an unrestricted grant from The Lundbeck Foundation.

POTENTIAL CONFLICT OF INTEREST: Dr Christensen has received honoraria, trip funding, and fees for participation in review activities from UCB Nordic and Eisai. The other authors have indicated they have no potential conflicts of interest to disclose.

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Pediatrics originally published online July 13, 2016;

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Pediatrics originally published online July 13, 2016;

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/early/2016/07/12/peds.2015-4654>

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