ARTICLE

Epilepsy, antiepileptic drugs, and serious transport accidents

A nationwide cohort study

Heléne E.K. Sundelin, PhD,* Zheng Chang, PhD,* Henrik Larsson, PhD, Paul Lichtenstein, PhD, Catarina Almqvist, PhD, Torbjörn Tomson, PhD, and Jonas F. Ludvigsson, PhD

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Correspondence
Dr. Sundelin
helene.sundelin@hotmail.com

Abstract

Objectives

To investigate the association between epilepsy and antiepileptic drugs and serious transport accidents requiring emergency care or resulting in death.

Methods

We identified 29,220 individuals 18 years or older with epilepsy without cerebral palsy or intellectual disability and 267,637 matched controls using Swedish registers. This nationwide cohort was followed from 2006 to 2013 for serious transport accidents. We used Cox regression to analyze the risk of serious transport accidents between individuals with epilepsy and matched controls, and then stratified Cox regression to compare the risk during periods of medication with the risk during nonmedication period within the same individual with epilepsy. We adjusted for civil status, employment, education, living area, psychiatric disorders prior to the start of follow-up, and psychotropic medication.

Results

Compared to matched controls, individuals with epilepsy were at increased risk of serious transport accidents (hazard ratio [HR] 1.37; 95% confidence interval [CI] 1.29–1.46). There were increased risks of pedestrian accidents (HR 2.24, 95% CI 1.69–2.97), bicycle accidents (HR 1.68, 95% CI 1.49–1.89) and car accidents (HR 1.31, 95% CI 1.19–1.44). However, among patients with a diagnosis of epilepsy, use of antiepileptic drugs did not influence the risk of serious transport accidents in population-level comparisons (HR 0.97; 95% CI 0.85–1.11) or within-individual comparisons (HR 0.99; 95% CI 0.69–1.42).

Conclusion

Serious transportation accidents were more common in individuals with epilepsy, but this risk was independent of use of antiepileptic drugs.

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*These authors contributed equally to this work.

From the Department of Pediatrics (H.E.K.S.), Linköping University Hospital; Departments of Medical Epidemiology and Biostatistics (Z.C., H.L., P.L., C.A., J.F.L.) and Clinical Neuroscience (T.T.), Karolinska Institutet; Astrid Lindgren Children's Hospital (C.A.), Karolinska University Hospital, Stockholm; Department of Pediatrics (J.F.L.), Örebro University Hospital, Sweden; Division of Epidemiology and Public Health, School of Medicine (J.F.L.), University of Nottingham, UK; and Department of Medicine (J.F.L.), Columbia University, New York, NY.

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Glossary

ACT = Anatomical Therapeutic Chemical Classification; **AED** = antiepileptic drug; **CI** = confidence interval; **HR** = hazard ratio; **ICD** = *International Classification of Diseases*; **NPR** = National Patient Register; **STA** = serious transport accidents.

Epileptic seizures can be associated with impaired awareness and uncontrolled motor activity affecting the ability to drive safely,[1] and also imposing risks for bicycle, motorcycle, or pedestrian accidents.[2] Restrictions for motor vehicle driving, which vary between countries, have been imposed on individuals with epilepsy, leading to important effects on everyday life.[3] Treatment with antiepileptic drugs (AEDs)[4,5] is for many a prerequisite for meeting the regulatory requirements for seizure control needed for driving, while on the other hand adverse effects of AEDs may impair driving abilities.[6,7] Adding to the complexity, individuals with epilepsy often have comorbidities, which can affect the ability to handle traffic.[8–10]

Most studies regarding epilepsy and risks associated with driving rely on self-reported car crashes, leading to inconsistent and inconclusive results.[11,12] Previous studies have focused on motor vehicle accidents, while data on accident risks for persons with epilepsy traveling on bicycle or other non-car-related accidents are scarce.

For the purpose of patient counseling and as a basis for recommendations on reasonable restrictions, there is an urgent need for more accurate and representative data on risks of traffic accidents in people with epilepsy. We have therefore carried out a nationwide cohort study of serious transport accidents (STA) in people with epilepsy utilizing Swedish health care registries, including motor vehicle as well as bicycle and pedestrian accidents. We have also assessed the effect of AEDs on STA.

Methods

Through Sweden's National Patient Register (NPR),[13] we identified all individuals born between 1960 and 1992 with ≥2 inpatient or outpatient diagnoses of epilepsy, according to the ICD-8 to ICD-10 (table e-1, links.lww.com/WNL/A286). Status epilepticus and febrile convulsions were not included in our definition of epilepsy (table e-1). Patients with a lifetime diagnosis of either cerebral palsy or intellectual disability (table e-1) were excluded, as these disorders pose an additional burden of comorbidity.

Study participants were followed between the second diagnosis of epilepsy, age 18 years, or July 1, 2006, whichever came last, and December 31, 2013, emigration, or death, whichever occurred first.

The main outcome measure was STA, defined as having an ICD-10 code of V01-V99 (table e-2, links.lww.com/WNL/A286) in the NPR or the Cause of Death Register, hence "serious" is defined as having an emergency visit at a hospital or death. The accidents were divided into the following groups: car (the coding does not distinguish between driver or passenger), motorcycle, bicycle, and pedestrian, all involving collision with a vehicle, or for pedestrian, accidents during transport (for a detailed description, see table e-2). We restricted traffic accidents to "emergency" (unplanned) hospital visits to rule out that a visit was due to rehabilitation for a previous traffic accident.

We obtained data on sociodemographic factors (marriage or registered partner, employment, education) and living area (urban vs countryside) from the Integrated Database for Labour Market Research (LISA).

Data on pharmacologic treatment were obtained through the Swedish Prescribed Drug Registry, which includes information on all dispensed medications since July 1, 2005, registered as Anatomical Therapeutic Chemical Classification (ACT) codes.[14] AEDs and psychotropic medication according to ACT codes are described in table e-3 (links.lww.com/WNL/A286). For the main analysis, all AEDs registered in Sweden were used. Information on psychiatric disorders was collected from the NPR.

We analyzed risks of STA in individuals with epilepsy using stratified Cox regression to calculate hazard ratios (HRs). Each patient with epilepsy was matched to up to 10 controls for sex and age at the year of diagnosis. Controls were selected from the Total Population Register.[15] Analyses were adjusted for sociodemographic factors, earlier psychiatric medication, and psychotropic medication. Study participants with missing values on sociodemographic factors and living area were excluded (309 patients with epilepsy and 26,358 controls) from the adjusted analysis. We estimated the excess number of accidents in patients with epilepsy. We analyzed individuals without any psychiatric disorders prior to the start of follow-up separately.

To investigate the association between AED and STA among individuals with epilepsy, we first used between-individual Cox regression and then stratified Cox regression with each individual entering as a separate stratum (within-individual analyses).[16] In the later approach, each patient served as his or her own control, and the rate of accidents during AED was compared to the same individual while untreated. AED treatment was included as a time-varying exposure.

Patients were defined as on treatment with AED if the interval between 2 dispensed AED prescriptions was ≤12 months. In case 2 prescriptions were more than 12 months apart, active

treatment was defined as the first 12 months after withdrawal of medication from the pharmacy.

In our sensitivity analysis, we compared 2 older AEDs (carbamazepine and oxcarbazepine) with 2 newer AEDs (levetiracetam and lamotrigine) as monotherapy. Further, we performed sensitivity analyses for the association between AEDs and STA in patients without any earlier psychiatric disorders prior to the start of follow-up.

In one of the sensitivity analyses, we used the 6 months cutoff to define treatment interval (instead of 12 months cutoff in the main analyses) to test whether the results were influenced by the choice of exposure (AED medication) definition.

Statistical analyses were conducted using SAS (SAS Institute, Cary, NC) software. HRs with 95% confidence intervals (CIs) that did not include 1.0 were regarded as statistically significant.

Standard protocol approvals, registrations, and patient consents

The study was approved by the Regional Ethics Review Board (2013/5:8), Stockholm, which adjudicated that individual informed consent was not required.[17]

Results

The study population consisted of 29,220 individuals with epilepsy and 267,637 controls (table 1). Among individuals with epilepsy, 24.1% had an earlier psychiatric disorder, compared to 6.3% of the controls (table 1). Antidepressants were the most common group of psychotropic medications (17.6%), followed by hypnotics/anxiolytics (15.0%), among individuals with epilepsy, compared to 5.6% and 3.0%, respectively, among controls (table 1). Of individuals with epilepsy, 75.3% received AEDs and 4.6% experienced at least one STA during follow-up compared to 3.4% of the controls (table 1). For further characteristics of the cohort, see table 1.

Table 1 Sample characteristics of patients with epilepsy and controls at baseline

	Epilepsy patients, n (%)			
	All	Female	Male	Controls, n (%)
Individuals at start of follow-up	29,220 (100)	14,642 (50.1)	14,578 (49.9)	267,637 (100)
At least one STA during follow-up	1,346 (4.6)	596 (4.1)	750 (5.1)	8,986 (3.4)
Death due to STA	8 (<0.1)	1 (<0.1)	7 (<0.1)	96 (<0.1)
Age groups, y				
18–25	8,744 (29.9)	4,373 (29.9)	4,371 (30.0)	80,131 (29.9)
26–35	8,595 (29.4)	4,437 (30.3)	4,158 (28.5)	78,683 (29.4)
36–45	9,539 (32.7)	4,765 (32.5)	4,774 (32.7)	87,523 (32.7)
46–53	2,342 (8.0)	1,067 (7.3)	1,275 (8.8)	21,300 (8.0)
Civil status, education, employment, and living area[a]				
Married or registered partner	6,632 (22.9)	3,883 (26.8)	2,749 (19.1)	66,062 (27.4)
In employment	15,756 (54.5)	7,839 (54.0)	7,917 (55.0)	163,270 (67.7)
In school	6,317 (21.8)	3,439 (23.7)	2,878 (20.0)	67,827 (28.1)
In metropolitan area	8,866 (30.7)	4,486 (30.9)	4,380 (30.4)	77,812 (32.3)
Earlier psychiatric comorbidity				
Any earlier psychiatric disorders	7,034 (24.1)	3,503 (23.9)	3,531 (24.2)	16,802 (6.3)
Psychotropic medication				
Antipsychotics	1,634 (5.6)	796 (5.4)	838 (5.8)	2,575 (1.0)
Hypnotics/anxiolytics	4,379 (15.0)	2,334 (15.9)	2,045 (14.0)	8,143 (3.0)
Antidepressants	5,153 (17.6)	2,974 (20.3)	2,179 (15.0)	14,944 (5.6)
ADHD medication	469 (1.6)	203 (1.4)	266 (1.8)	778 (0.3)

Abbreviations: ADHD = attention-deficit/hyperactivity disorder; STA = serious traffic accidents.
[a] A total of 184 male and 125 female patients and 26,358 controls had missing values on civil status, education, employment, and living area.

Table 2 Association between epilepsy and serious transport accidents (STA) in Swedish adults

	Person-years at risk, n		No. of accidents, n		Crude association, HR[a] (95% CI)	Adjusted association, HR[a] (95% CI)	Estimated increased no. of accidents per year in people with epilepsy (95% CI)
	Epilepsy patients	Controls	Epilepsy patients	Controls			
All STA							
All	165,506	1,851,158	1,346	8,986	1.68 (1.59–1.78)	1.37 (1.29–1.46)	297.3 (233.0–369.6)
Men	81,426	914,818	750	5,108	1.65 (1.52–1.78)	1.32 (1.22–1.44)	145.5 (100.0-200-0)
Women	84,079	936,340	596	3,878	1.73 (1.58–1.88)	1.44 (1.31–1.58)	153.2 (108.0–202.0)
All STA in people without any earlier psychiatric disorders							
All	130,518	1,738,169	925	8,019	1.53 (1.42–1.64)	1.37 (1.27–1.47)	222.8 (162.6–283.0)
Men	64,377	866,091	508	4,591	1.45 (1.32–1.60)	1.31 (1.19–1.44)	105.8 (64.8–150.2)
Women	66,141	872,078	417	3,428	1.63 (1.46–1.81)	1.45 (1.30–1.61)	117.0 (78.0–158.6)
Car accidents							
All	168,006	1,869,015	557	3,846	1.59 (1.46–1.74)	1.31 (1.19–1.44)	107.2 (65.7–152.1)
Men	82,778	925,428	304	2,081	1.62 (1.43–1.83)	1.30 (1.15–1.48)	55.8 (27.9–89.3)
Women	85,228	943,588	253	1,765	1.57 (1.37–1.79)	1.31 (1.14–1.50)	49.4 (22.3–79.7)
Motor cycle accidents							
All	169,234	1,877,547	199	1,385	1.59 (1.37–1.85)	1.22 (1.04–1.43)	27.5 (5.0–53.7)
Men	83,321	928,398	160	1,189	1.48 (1.26–1.75)	1.14 (0.96–1.36)	14.9 (-4.3–38.4)
Women	85,912	949,149	39	196	2.30 (1.62–3.26)	1.74 (1.20–2.52)	13.1 (13.1–27.0)
Bicycle accidents							
All	168,706	1,875,714	380	2,177	2.00 (1.80–2.24)	1.68 (1.49–1.89)	133.1 (95.9–174.3)
Men	83,208	928,867	209	1,248	1.92 (1.66–2.24)	1.59 (1.36–1.86)	66.0 (40.2–96.1)
Women	85,497	946,847	171	929	2.12 (1.80–2.51)	1.80 (1.51–2.14)	67.1 (42.8–95.6)
Pedestrian accidents							
All	169,662	1,881,890	78	285	3.13 (2.42–4.06)	2.24 (1.69–2.97)	31.9 (17.7–50.6)

Continued

Table 2 Association between epilepsy and serious transport accidents (STA) in Swedish adults *(continued)*

	Person-years at risk, n		No. of accidents, n		Crude association, HR[a] (95% CI)	Adjusted association, HR[a] (95% CI)	Estimated increased no. of accidents per year in people with epilepsy (95% CI)
	Epilepsy patients	Controls	Epilepsy patients	Controls			
Men	83,698	932,431	41	158	3.07 (2.15–4.37)	2.00 (1.34–3.00)	14.2 (4.8–28.4)
Women	85,964	949,459	37	127	3.21 (2.20–4.67)	2.56 (1.71–3.84)	17.9 (8.2–32.7)

Abbreviations: CI = confidence interval; HR = hazard ratio.
[a] HR were adjusted for civil status, education, employment, living area, earlier psychiatric disorders, and psychotropic medication. The estimated increased number of accidents was calculated as $I_0 \times (HR_a - 1) \times N_e$, for which I_0 is the unadjusted event rate in the unexposed group, HR_a is the adjusted HR, and N_e is the number of exposed people.

Fewer than 0.1% of epilepsy patients and their controls died from STA during follow-up (table 1).

Individuals with epilepsy showed significantly higher rates of STA than those without epilepsy (table 2); the unadjusted HR was 1.68 (95% CI 1.59–1.78). Adjusting for confounders, the HR was 1.37 (95% CI 1.29–1.46), with no difference between men and women (table 2).

Epilepsy was linked to a 2.2-fold increased risk of pedestrian accidents (HR 2.24, 95% CI 1.69–2.97), a 1.7-fold risk of bicycle accidents (HR 1.68, 95% CI 1.49–1.89), and finally a 1.3-fold increased risk of car accidents (HR 1.31, 95% CI 1.19–1.44) (table 2). The increased number of accidents per year in individuals with epilepsy was 297.3 (95% CI 233.0–369.6) (table 2). Table 2 presents additional data.

We found no significant differences in accidents rates among individuals with epilepsy during periods with AED medication compared to periods without, in the within-individual comparison or in the population-level comparison (table 3).

The HRs of STA in patients with levetiracetam/lamotrigine monotherapy or on oxcarbazepine/carbamazepine monotherapy were not different from the main analysis (table 4).

Discussion

In this nationwide cohort study of over 29,000 individuals with epilepsy, we found a 37% increased risk of STA. The risk increase was especially high in cyclists and pedestrians. We found no association between AED treatment and risk of STA.

Our findings of an excess risk of car accidents are in line with earlier data, including a Danish study that found that drivers with epilepsy are more often treated at an emergency department after a motor vehicle accident.[18] A French study based on national databases found that drivers exposed to AEDs (n = 251) had an increased risk of being responsible for a crash (OR 1.74, 95% CI 1.29–2.34) and concluded that the increased risk was more likely related to seizures than the effect of AEDs.[19] Another record linkage study on long-term chronic disease and transportation accidents, including 80 individuals with epilepsy, found a 2.5-fold increased risk for crash responsibility in patients with epilepsy.[20] However, contradictory data exist (no association with accidents) based on self-reported[3,11,12,21] and register-based data.[22] One reason for the lack of association in the Canadian article could be lack of study power, as their adjusted OR was 1.38 (95% CI 0.97–1.96).[22] Their study included 10,240 individuals with epilepsy as compared to almost 3 times as many in our study.[22]

In the current study, the risk of STA was similar in men and women with epilepsy. This is in line with the increased risk of

Table 3 Association between antiepileptic drug medication and serious transport accidents in patients with epilepsy

Patients with epilepsy	Person-years at risk, n		No. of accidents		Population-level comparison,[a] HR (95% CI)	Within-individual comparison, HR (95% CI)
	Periods with medication	Periods without medication	Periods with medication	Periods without medication		
All	106,276	63,609	1,119	671	0.97 (0.85–1.11)	0.99 (0.69–1.42)
Male	51,885	31,931	674	375	1.08 (0.91–1.29)	0.92 (0.58–1.47)
Female	54,392	31,678	445	296	0.85 (0.70–1.03)	1.09 (0.62–1.92)

Abbreviations: CI = confidence interval; HR = hazard ratio.
[a] Population-level comparisons were adjusted for civil status, education, employment, living area, earlier psychiatric disorders, and psychotropic medication. Within-individual comparisons were adjusted for all factors that are constant within each individual during the follow-up.

accidents in patients with diabetes, where sex has no significant influence on the collision risk,[23] even though male drivers in general have an increased risk of accidents.[24] The frequency of female drivers varies considerably between different countries and cultures. In Sweden, sex differences are small, which reinforces our result that there is no biological effect of sex when it comes to STA for individuals with epilepsy.

The associations between epilepsy and STA could not be fully explained by comorbid psychiatric disorders; hence it is probably epilepsy as such that is the main reason for the increased risk.

We found a 2.2-fold risk of pedestrian STA among epilepsy patients, which is consistent with a previous study that found a more than 2-fold risk of injuries in street accidents as well as an overall increased risk of accidents in epilepsy patients.[2]

In our study, approximately 25% of individuals with epilepsy were not on medication during follow-up. This likely represents, to a large extent, patients whose epilepsy is in remission or resolved, and for whom medication has been withdrawn. Another explanation might be nonadherence to AED treatment, as this is common (between 26% and 50% in one study).[25,26]

Both scenarios could explain why we did not find any association between STA and medication status, not even in the within-patient analysis, where each individual with epilepsy served as his or her own control. We did not find any difference in the comparison between carbamazepine/oxcarbazepine and levetiracetam/lamotrigine; nor did Orriols et al.[19] find any difference in STA risk according to AED class.

Strengths

This is the largest study on epilepsy and STA so far, and with increased statistical power we were able to demonstrate small risk differences. We used the NPR to ascertain epilepsy; this register has been used before to define epilepsy.[27,28] Hence this population-based study includes all individuals with epilepsy 18 years or older, except for those with comorbid cerebral palsy and intellectual disability, in Sweden. In this way, all types and severities of epilepsy are included, reflecting their occurrence in the population. Several previous studies may potentially suffer from selection bias as only certain subgroups of epilepsy patients have been included.[11,12] Different methods have been used to report accidents in individuals with epilepsy, from reporting over shorter time intervals to lifetime accident rates.[11,12] In our approach, we calculated the risk in comparison to matched controls and also reported adjusted

Table 4 Subgroup analyses and sensitivity analyses for the association between antiepileptic drugs and transport accidents

Treatment periods	Cohort	Patients with epilepsy, n	Number of accidents	Population-level comparison, HR (95% CI)	Within-individual comparison, HR (95% CI)
Defined using a 6-mo cutoff	Full cohort	29,220	1,790	0.98 (0.86–1.11)	0.94 (0.71–1.26)
Defined using a 12-mo cutoff	Patients with carbamazepine or oxcarbazepine monotherapy	5,002	204	0.81 (0.57–1.15)	2.03 (0.50–8.26)
	Patients with lamotrigine or levetiracetam monotherapy	3,700	172	0.50 (0.09–2.62)	0.50 (0.09–2.62)
	Patients without any earlier psychiatric disorder	22,186	1,193	1.06 (0.90–1.25)	0.79 (0.46–1.34)

Abbreviations: CI = confidence interval; HR = hazard ratio.
Population-level comparisons were adjusted for marriage, employment, education, living area, earlier psychiatric disorders, and psychotropic medication (antipsychotics, hypnotics/anxiolytics, antidepressants, and attention-deficit/hyperactivity disorder medication). Within-individual comparisons were adjusted for all factors that are constant within each individual during the follow-up.

results. Our within-individual analyses regarding medication with AED, or not, allowed us to adjust for potential unmeasured but important confounders such as type and severity of epilepsy, mental and motor abilities, genetic predisposition, and somatic comorbidities. To our knowledge, our study is the first to examine all types of STA.

Limitations

Our study had some limitations. None of the registers used had information on driver's license ownership, if the epilepsy patients were actually driving, and whether they were actually responsible for the accident. These circumstances were the same for individuals with epilepsy and our controls. Previous studies regarding epilepsy and driving have shown that 73% of individuals with epilepsy have a driver's license, compared to 94% of the general adult population.[3] However, through excluding individuals with comorbid cerebral palsy and intellectual disability, the proportion of driver's license holders probably increased. Still, the lower proportion of potential drivers among epilepsy patients may have diluted the association between epilepsy and STA.

A further limitation of the study is the lack of information on seizure control among the epilepsy patients, which also complicates the interpretation of associations with AED treatment. Those who are off medication may be so because their epilepsy is resolved and thus less exposed to risks imposed by seizures.

As our outcome was transport accidents that resulted in emergency hospital visits or death, minor accidents were not included. We cannot rule out that patients with epilepsy who regularly visit hospitals for their chronic disease are more prone to seek care for accidents and if so, this would drive up our risk estimates.

As our findings are based on a cohort living in Sweden, a country with small costs for health care, reduced costs for medication, and a rather low general rate of transport accidents, generalizations across cultures/countries should be made with caution, also taking into account the Swedish requirements for driver's licenses.

Interpretations

Individuals with epilepsy are at a moderately increased risk of STA, and AED medication does not seem to influence that risk. We cannot determine to what extent the increased risk is seizure-related, but other studies have shown that the majority of car crashes in individuals with epilepsy are not caused by a seizure,[29,30] although accidents in general seem to be.[2] In comparison to individuals with diabetes, where the only link to an increased risk of collisions is hypoglycemia[23] (introduced by medication), the increased risk in epilepsy patients does not seem to be associated with medication or earlier psychiatric comorbidity.

To regulate driving is not easy as such regulations aim to maximize public safety while preserving individual freedom as much as possible.[31] Studies have shown that the length of seizure freedom is important, yet the shortening of these periods has not led to more accidents.[32] In Sweden, individuals with epilepsy must have been seizure-free the last 12 months, following the regulations being implemented in the European union.[33] Many individuals with epilepsy are driving regardless of whether they are allowed to, and the reporting of these patients is low.[34,35] However, mandatory reporting of patients by their physician has not been shown to reduce the risk of accidents.[3]

Bicycle accidents in the general population are a growing problem as cycling becomes increasingly popular,[36] which is probably true also for individuals with epilepsy. The increased risk of 70% should have implications both for implementations of safety measures and counseling of individuals with epilepsy. Our results raise the same concern for pedestrians with epilepsy.

There is a significantly increased risk for STA in individuals with epilepsy. This increased risk does not seem to be influenced by sex. It is of importance to further investigate the circumstances that contribute to this increased risk of STA among individuals with epilepsy. With that knowledge, it might be possible to educate individuals with epilepsy about preventive measures rather than implement stricter regulations.

Author contributions

Heléne E.K. Sundelin: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval. Zheng Chang: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval, statistical analysis. Henrik Larsson: drafting/revising the manuscript, accepts responsibility for conduct of research and final approval, acquisition of data, study supervision, obtaining funding. Paul Lichtenstein: drafting/revising the manuscript, study concept or design, accepts responsibility for conduct of research and final approval, acquisition of data, obtaining funding. Catarina Almqvist: drafting/revising the manuscript, accepts responsibility for conduct of research and final approval, acquisition of data, obtaining funding. Torjörn Tomson: drafting/revising the manuscript, analysis or interpretation of data, accepts responsibility for conduct of research and final approval. Jonas F. Ludvigsson: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and final approval.

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Epilepsy, antiepileptic drugs, and serious transport accidents

A nationwide cohort study

Heléne E.K. Sundelin, PhD, Zheng Chang, PhD, Henrik Larsson, PhD, Paul Lichtenstein, PhD, Catarina Almqvist, PhD, Torbjörn Tomson, PhD, and Jonas F. Ludvigsson, PhD

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Correspondence
Dr. Sundelin
helene.sundelin@hotmail.com

Study question

Are epilepsy and the use of antiepileptic drugs (AEDs) related to serious transport accidents (STAs)?

Summary answer

Epilepsy increases the risk of STAs, and this effect is independent of the use of AEDs.

What is known and what this paper adds

Epilepsy can impair safe driving, but most past studies have analyzed self-reported car crashes while ignoring non-car STAs, such as bicycle STAs. This study elucidates the association between epilepsy and STAs with nationwide Swedish registry data that include non-car STAs.

Participants and setting

This study identified 29,220 patients with epilepsy without cerebral palsy or intellectual disability in Sweden's National Patient Register who were born between 1960 and 1992. Each patient was matched by sex and age to ≤10 healthy controls drawn from the Total Population Register, resulting in 267,637 healthy controls.

Design, size, and duration

Study participants were followed from the second epilepsy diagnosis, the 18th birthday, or July 1, 2006, whichever occurred last, until emigration, death, or December 31, 2013, whichever occurred first. Outcomes data were obtained from the National Patient Register and the Cause of Death Register. Prescriptions data were obtained from the Swedish Prescribed Drug Registry.

Main results and the role of chance

The occurrence of at least one STA was recorded for 1,346 (4.6%) patients and 8,986 (3.4%) healthy controls. This meant that the patients were at higher risk of STAs (adjusted hazard ratio, 1.37; 95% CI, 1.29–1.46). This was true for STAs of the car, bicycle, motorcycle, and pedestrian subtypes (see table). Of the patients, 75.3% received AEDs. The study found no difference in STA rates between AED-treated and untreated periods (within-individual comparison, hazard ratio, 0.99; 95% CI, 0.69–1.42).

STA subtype	Adjusted hazard ratio (95% CI)
Car	1.31 (1.19–1.44)
Motorcycle	1.22 (1.04–1.43)
Bicycle	1.68 (1.49–1.89)
Pedestrian	2.24 (1.69–2.97)

Bias, confounding, and other reasons for caution

It is unclear whether the participants were drivers or passengers during car STAs. There were no data on seizure control or minor accidents not requiring medical attention.

Generalizability to other populations

Sweden has low healthcare costs and a low general STA rate. This may limit generalizability to other countries and cultures.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

