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Do recurrent seizure-related head injuries affect seizures in people with epilepsy?

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Abstract

Seizure-related head injuries (SRHIs) are among the most commonly encountered injuries in people with epilepsy (PWE). Whether head injury has an effect on preexisting epilepsy is not known. The purpose of this study was to systematically assess for any possible effects of SRHIs on seizure frequency and seizure semiology over a 2-year period. We identified 204 patients who have been followed at the Baylor Comprehensive Epilepsy Center from 2008 to 2010. SRHI occurred in 18.1% of the cohort. Most injuries (91%) were classified as mild. Though seizure frequency varied following head injury, overall seizure frequency was not significantly impacted by presence or absence of SRHI over the 2-year study period. Changes in seizure semiology were not observed in those with SRHIs. Although mild SRHI is common among PWE, it does not appear to have an effect on seizure characteristics over a relatively short period.

Keywords

Epilepsy; Seizure; Head injury

1. Introduction

People with epilepsy (PWE) are at an increased risk of injury compared with the general population, and most injuries are seizure related [1]. Although it has been established that seizure-related head injuries (SRHIs) make up many of the injuries encountered by PWE [1–4], the long-term effects of recurrent SRHIs on seizure severity are not known. Head injury is universally recognized as one of the major risk factors for developing epilepsy, and accounts for more than 20% of symptomatic epilepsy and 5% of all epilepsy [5]. Though the relative risk of developing posttraumatic epilepsy is associated with injury severity, even mild head injury increases the subsequent risk of epilepsy by about 50% [6]. A myriad of biochemical changes encountered in head injury are potentially responsible for development of epilepsy. Epileptogenesis may be related to the toxic effects of hemoglobin breakdown products on neuronal function associated with intracranial hemorrhages, such as focal

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6. Ethical approval

This study was approved by the appropriate ethics committee and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

contusions [7]. Closed head injury also often produces diffuse axonal injury, which is associated with edema, ischemia, and secondary cellular damage through the release of toxic mediators, such as cytokines and excitatory amino acids [8], which may contribute to epileptogenicity. The physiological changes triggered by trauma responsible for developing epilepsy de novo may conceivably exacerbate preexisting epilepsy. Indeed, a close chronological association between mild head injury and worsening of seizure control was observed within days of injury in a series of five patients [9].

Most studies on seizure-related injury are retrospective, are cross-sectional, inquire about past events, and involve indirect methods, such as questionnaires and medical record documentation [10]. Thus, there is little information on the possible relationship between SRHI and its potential effect on seizure characteristics, be it transient or chronic. Since 2008, seizure-related injury data have been obtained habitually over relatively fixed intervals at the Baylor Comprehensive Epilepsy Center. The purpose of this study was to determine whether SRHI has an effect on epilepsy characteristics, such as seizure frequency and semiology, over a 2-year period when assessed systematically.

2. Methods

Data are from an ongoing longitudinal study of adults with epilepsy, systematically investigating for seizure-related injury at each follow-up visit to the Baylor Comprehensive Epilepsy Center (BCEC) in Houston, TX, USA [4]. Injuries assessed at each patient visit included seizure-related and non-seizure-related events. Injuries were defined as any dysfunction or pain resulting from an accidental occurrence. Injury severity classification was based on a prior scale [6], where mild SRHI was defined as consciousness impairment or amnesia lasting less than 30 minutes with no fracture; moderate as consciousness impairment or amnesia lasting 30 minutes to 24 hours or skull fracture; and severe as consciousness impairment or amnesia lasting more than 24 hours, intracranial hematoma, or brain contusion. BCEC is a tertiary epilepsy center and patients receiving care there are typically referred for pharmacoresistant seizures. We identified a retrospective cohort of 204 adult PWE seen at the BCEC in 2008 and followed through 2010.

2.1. Statistical analysis

The following statistical analyses were performed using R Version 2.13.1 (R Foundation, Vienna, Austria). Associations were evaluated at the $\alpha=0.05$ level.

2.1.1. Demographic characteristics of SRHI versus non-SRHI groups—

Differences in age and epilepsy duration were estimated using an unpaired Student two-sample *t* test of a difference in means. To account for the skewness of seizure frequency, differences in mean seizure frequencies were estimated using an unpaired Student two-sided *t* test on the log transform of seizure frequencies. Differences in categorical variables (e.g., gender, seizure classification, seizure localization, and whether the patient experienced recurrent seizures) were estimated using a Z test of two proportions based on the assumption of normality, with the exception of multifocal localization, other localization-related epilepsy, and idiopathic classification, which were estimated using a one-sided Fisher's

exact test due to low cell counts. Differences in seizure semiology were also estimated using Fisher's exact test due to low cell counts.

2.1.2. Changes in seizure frequency—To examine the effect of SRHI on the progression of seizure frequency over time, seizure frequencies at 6-month intervals over a 2-year study period were obtained. Seizure frequency progression rates were calculated for each 6-month interval (i.e., from 0 to 6 months, 6 to 12 months, 12 to 18 months, and 18 to 24 months) as the change in seizure frequency over the interval, and averaged over the 2-year study period for each individual (for the non-SRHI group) or over the period pre- and postinjury (for the SRHI group) to yield average 6-month seizure frequency progression rates for each individual. Differences in the average seizure frequency progression rate for the SRHI group pre- and postinjury, versus that of the non-SRHI group, were estimated using an unpaired Student two-sided t test. The pooled variance was employed in comparing pre-injury SRHI and non-SRHI groups, whereas the Welch approximation to the degrees of freedom was employed in comparing post-injury SRHI and non-SRHI groups because of nonequality of variances in the latter case. Differences in the variability of the seizure frequency rates of change were estimated using a test of $H_0: \sigma_X^2 / \sigma_Y^2 = 1$ against the alternative $H_1: \sigma_X^2 / \sigma_Y^2 \neq 1$, where under H_0 , $\frac{S_X^2}{S_Y^2}$ has an F distribution with $r_1 = n - 1$ and $r_2 = m - 1$ degrees of freedom, and n and m are the number of observations in X and Y , respectively.

3. Results

A total of 204 patients were followed during the study period, allowing for continued follow-up assessment of seizure-related injury and potential effects on seizure frequency and semiology during each visit in clinic. Of these patients, 37 (18.1%) experienced SRHI during the 2-year study period. A total of 43 SRHIs were documented. Five patients experienced multiple SRHIs. Thirty-nine (91%) head injuries were classified as mild and 4 (9%) as moderate, based on criteria defined in prior studies [6]. No injuries classified as severe occurred during the study period. Six injuries required evaluation in the emergency room, and head CT scans did not reveal any acute abnormalities. One patient experienced non-seizure-related mild head injury during a contact football game. No other non-seizure-related head injuries occurred during the study period.

3.1. Demographic characteristics

Mean age, proportion of multifocal epilepsy, baseline seizure frequency, and the proportion experiencing recurrent seizures were found to differ significantly between SRHI and non-SRHI groups ($P=0.025$, $P<0.001$, $P<0.001$, $P=0.04$) (Table 1). The proportion of patients experiencing tonic-clonic seizures alone, along with the proportion experiencing a combination of tonic, atonic, myoclonic, and tonic-clonic seizures, was also found to differ significantly between groups ($P=0.02$, $P=0.009$) (Table 1). No other demographic or seizure characteristic variables were found to differ significantly between the SRHI and non-SRHI groups.

4. Changes in seizure frequency or semiology

The progression rate of seizure frequencies over the 2-year study period was not found to differ significantly between patients who did not experience SRHI and patients who did experience SRHI, either before or after the injury ($P=0.518$ and $P=0.4871$, Table 2A). However, the seizure frequency progression rates for the SRHI group postinjury were found to have a significantly higher variability than those of the non-SRHI group, whereas the variability of the progression rates was not found to be significantly different between the groups prior to head injury ($P<0.01$ and $P>0.05$) (Table 2B). No changes in seizure semiology occurred for either group over 2 years.

5. Discussion

In epilepsy, seizure remissions and recurrences are common with many potential contributing factors [11]. The ability to predict which seizure characteristics affect seizure outcomes allows treating physicians to understand and discuss these factors with patients. To date, this is the first study, to our knowledge, that systematically assessed for possible effects of SRHI on seizures. Our data present a 2-year view of seizure outcomes and their relationship to recurrent SRHIs. In the current study, we report that though mild SRHI is common among PWE, it does not appear to have a sustained effect on seizure characteristics over a relatively short period.

At baseline, those with recurrent injuries had more seizures than those without. This is consistent with prior reports, where seizure frequency is often considered the strongest risk factor for seizure-related injury [2–4,10]. Among those with recurrent SRHIs, a substantial change in the variability of seizure frequency progression rates was seen after the injury, suggesting that head injury may cause a decrease in predictability of seizure frequency in the short term. Nevertheless, seizure frequency progression did not significantly differ either prior to or after the injury from progression in patients without head injury, suggesting that SRHI does not affect the overall progression of preexisting epilepsy in the short term.

Our study has clear limitations. The 2-year time frame we used for the study period was relatively limited. Because posttraumatic epilepsy may manifest up to decades following injury [6] with a wide range of patterns of evolution and prognosis, 2 years may be too short a period to adequately address the potential exacerbating properties of SRHI on epilepsy. Another limitation is the fact that the 6-month epochs may have been too long to detect transient effects on seizure frequency. We also did not specifically assess antiepileptic drug changes between the groups, thereby introducing a potential confounding issue, as changes in medications may have led to differences in seizure frequency, thus leading one group to be subjected to more head injuries. In addition, the sample size may be too small, as the seminal study reporting head injury as a risk for developing seizures required more than 4000 subjects [6]. However, this article represents the largest sample and longest period of investigation to date regarding the risk for exacerbating preexisting epilepsy resulting from SRHI. One previous case series described worsening of seizures in five patients within days of mild head injuries [9]. In our study, no such changes were reported. Nearly all injuries involved in the study were characterized as mild. Though mild head injury represents a risk

factor for unprovoked seizures within the first 4 years following injury, the risk of developing epilepsy is proportional to the severity of the injury encountered [6]. The fact that most injuries were mild introduces selection bias, which can partly explain the lack of effect on seizure frequency. Nevertheless, no changes in seizure frequency or seizure semiology occurred in any of the patients studied during the 2-year study period.

Historically, physical limitations have been imposed on PWE primarily out of concern for safety. Experiencing a seizure while engaging in physical activity can lead to falls or impairment of one's ability to respond to danger and makes one susceptible to injury. In addition to the inherent dangers, head injury also often affects subjective health. Mild head injury can lead to such complaints as persistent headaches, memory impairment, mood disorders, and disability [12–15], which in turn lead to diminished health-related quality of life [16]. Though recurrent injuries affected short-term seizure frequency variability, the concern that mild SRHI might precipitate or exacerbate seizures appears small based on the findings of our study. Whether SRHI affects the natural course and outcomes among PWE over a long period is not known and requires further study.

References

1. Beghi E, Cornaggia C. for the RESt-1 Group. Morbidity and accidents in patients with epilepsy: results of a European cohort study. *Epilepsia*. 2002; 43:1076–83. [PubMed: 12199734]
2. Buck D, Baker GA, Jacoby A, Smith DF, Chadwick DW. Patients' experiences of injury as a result of epilepsy. *Epilepsia*. 1997; 38:439–44. [PubMed: 9118849]
3. Neufeld MY, Vishne T, Chistik V, Korczyn AD. Life-long history of injuries related to seizures. *Epilepsy Res*. 1999; 34:123–7. [PubMed: 10210026]
4. Friedman DE, Tobias RS, Akman CI, Smith EO, Levin HS. Recurrent seizure-related injuries in people with epilepsy at a tertiary epilepsy center: a two year longitudinal study. *Epilepsy Behav*. 2010; 19:400–4. [PubMed: 20851687]
5. Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota: 1940–1980. *Epilepsia*. 1991; 32:429–45. [PubMed: 1868801]
6. Annegers JF, Hauser WA, Coan RP, Rocca WA. A population based study of seizures after traumatic brain injury. *N Engl J Med*. 1998; 338:20–4. [PubMed: 9414327]
7. Willmore LJ. Post-traumatic epilepsy: cellular mechanisms and implications for treatment. *Neurology*. 1991; 31(Suppl 3):S67–73.
8. Meythaler LM, Peduzzi JD, Eleftheriou E, Novack TA. Current concepts: diffuse axonal injury—associated traumatic brain injury. *Arch Phys Med Rehabil*. 2001; 82:1461–71. [PubMed: 11588754]
9. Tai PC, Gross DW. Exacerbation of pre-existing epilepsy by mild head injury: a five patient series. *Can J Neurol Sci*. 2004; 31:394–7. [PubMed: 15376487]
10. Friedman DE, Gilliam FG. Seizure-related injuries are underreported in pharmacoresistant localization-related epilepsy. *Epilepsia*. 2010; 51:43–7. [PubMed: 19519796]
11. Choi H, Heiman G, Pandis D, et al. Seizure remission and relapse in adults with intractable epilepsy: a cohort study. *Epilepsia*. 2008; 49:1440–5. [PubMed: 18410367]
12. Zhang S, Carroll LJ, Cassidy JD, Paniak C. Factors influencing self-rated health in traffic-related mild traumatic brain injury. *J Rehabil Med*. 2009; 41:1062–7. [PubMed: 19894002]
13. Collins MW, Grindel SH, Lovell MR, et al. Relationship between concussion and neuropsychological performance in college football players. *JAMA*. 1999; 282:964–70. [PubMed: 10485682]
14. Teasdale TW, Engberg AW. Cognitive dysfunction in young men following head injury in childhood and adolescence: a population study. *J Neurol Neurosurg Psychiatry*. 2003; 74:933–6. [PubMed: 12810783]

15. Wall SE, Williams WH, Cartwright-Hatton S, et al. Neuropsychological dysfunction following repeat concussions in jockeys. *J Neurol Neurosurg Psychiatry*. 2006; 77:518–20. [PubMed: 16543534]
16. Alexander MP. Neuropsychiatric correlates of persistent postconcussive syndrome. *J Head Trauma Rehabil*. 1992; 7:60–9.

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Table 1

Comparison of demographic and seizure characteristics between the SRHI and non-SRHI groups.

	$\bar{x}(\bar{SE})$ or $p(\bar{SE})$		<i>P</i> value
	SRHI (<i>n</i> =37)	Non-SRHI (<i>n</i> =167)	
Demographic			
Age	31.3 (2.3)	37.1 (1.1)	0.025
Female (ref: male)	54.1% (8.2%)	52.1% (3.9%)	0.83
Seizure characteristics			
Classification			
Idiopathic ^a	5.4% (3.7%)	10.2% (2.3%)	0.32
Symptomatic	35.1% (7.9%)	37.7% (3.8%)	0.78
Cryptogenic	59.5% (8.1%)	52.1% (3.9%)	0.42
Localization			
Multifocal ^a	8.1% (4.5%)	0.0% (0.0%)	<0.001
Generalized epilepsy	29.7% (7.5%)	34.1% (3.7%)	0.61
Temporal lobe epilepsy	43.2% (8.1%)	41.9% (3.8%)	0.88
Frontal lobe epilepsy	16.2% (6.1%)	16.8% (2.9%)	0.93
Other ^a	2.7% (2.7%)	7.2% (2.0%)	0.31
Semiology ^a			
Absence	0.0% (0.0%)	0.6% (0.6%)	0.82
Dialeptic	43.2% (8.1%)	40.1% (3.8%)	0.43
Hypermotor	10.8% (5.1%)	3.6% (1.4%)	0.085
Focal motor	2.7% (2.7%)	9.6% (2.3%)	0.15
Tonic-clonic seizures alone	18.9% (6.4%)	37.7% (3.8%)	0.02
Tonic, atonic, myoclonic, tonic-clonic	24.3% (7.1%)	8.4% (2.1%)	0.009
Seizure frequency (per month)	0.47 (0.13) ^b	−0.120 (0.079) ^b	<0.001
Epilepsy duration (in years)	22.3 (2.1)	19.5 (1.05)	0.24
Recurrent seizures	91.9% (4.5%)	79.6% (3.1%)	0.04

^aFisher's exact test.^bLog of geometric mean.

Table 2

Comparison of mean seizure frequency progression rates and their variability between the SRHI and non-SRHI groups.

A. Seizure frequency progression rates		
	$x(\text{\$}E)$	P
SRHI pre-injury vs non-SRHI		
SRHI pre-injury ($n=37$)	-0.460 (3.633)	0.518
Non-SRHI ($n=167$)	-0.904 (3.587)	
SRHI postinjury vs non-SRHI		
SRHI postinjury ($n=37$)	-2.220 (11.127)	0.487
Non-SRHI ($n=167$)	-0.904 (3.587)	

B. Variability in rates		
	F	P
SRHI pre-injury vs non-SRHI	1.026	>0.05
SRHI postinjury vs non-SRHI	9.622	<0.01