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Prevalence of epileptic and nonepileptic events after pediatric traumatic brain injury

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ABSTRACT

Though posttraumatic epilepsy (PTE) is a prominent sequela of traumatic brain injury (TBI), other nonepileptic phenomena also warrant consideration. Within two UCLA pediatric TBI cohorts, we categorized five spell types: 1) PTE; 2) Epilepsy with other potential etiologies (cortical dysplasia, primary generalized); 3) Psychopathology; 4) Behavior misinterpreted as seizures; and 5) Other neurologic events. The two cohort subsets differed slightly in injury severity, but they were otherwise similar. Overall, PTE occurred in 40%, other epilepsy etiologies in 14%, and nonepileptic spells collectively in 46%. Among children with spells, PTE was associated with severe TBI ($p = 0.001$), whereas psychopathology ($p = 0.014$) and epilepsy with other etiologies ($p = 0.006$) were associated with milder TBI severity. Posttraumatic epilepsy ($p = 0.002$) and misinterpreted behavior ($p = 0.049$) occurred with younger injury age. Psychopathology ($p = 0.020$) and other neurologic events ($p = 0.002$) occurred with older injury age. In evaluating possible PTE, clinicians should maintain a broad differential diagnosis to prevent misdiagnosis and inappropriate treatment.

1. Introduction

Traumatic brain injury (TBI) affects more than 475,000 children under 15 years of age annually, with the highest rates observed in children aged 0–4 and a second peak in adolescence [1,2]. Traumatic brain injury is a well-known risk factor for epilepsy, with the incidence of seizures increased seventeen-fold after severe TBI and by a factor of 1.5 even after mild TBI without skull fracture or prolonged loss of consciousness [3]. The risk for epilepsy remains elevated even ten years after injury [4]. Given these epidemiologic findings, clinicians often approach the evaluation of paroxysmal events in a child with a history of TBI with a heightened index of suspicion for epilepsy. In addition to posttraumatic epilepsy (PTE), other neurologic symptomatologies, such as postconcussive migraines and cognitive deficits, are often emphasized in the differential diagnosis of post-TBI "spells" [3,5–8].

However, a number of neuropsychiatric sequelae may also complicate recovery from pediatric TBI, including various episodic nonepileptic phenomena characterized by paroxysmal movements, unusual sensations, and staring. Pediatric TBI is associated with an increased risk of psychiatric diagnoses, including depression, posttraumatic stress disorder, panic disorder, obsessive–compulsive disorder, and attention deficit hyperactivity disorder (ADHD) [9–11]. In one analysis, 46% of children suffering from TBI developed new-onset mood or anxiety disorders within 6 months of TBI, in comparison to 14% of controls with solely orthopedic injuries [12].

The occurrence of nonepileptic posttraumatic events is well-established in the adult TBI literature. A total of 33% of adults with a history of moderate to severe TBI admitted for video-EEG characterization of paroxysmal "spells" were diagnosed with nonepileptic events [13]. Conversely, 24–32% of adults with video-EEG-confirmed nonepileptic events attributed their "seizures" to a head injury, which had usually occurred less than 1 year prior to the onset of their spells [14,15]. Similar analyses have not been conducted in the pediatric TBI population. Therefore, we sought to explore if paroxysmal "spells" presenting in children with a history of TBI would similarly reflect a high frequency of nonepileptic symptomatology.

The goal of this study was to compare the nature of paroxysmal events in two cohorts of pediatric TBI patients evaluated at the University of California Los Angeles (UCLA) Pediatric TBI center. Both early and late posttraumatic seizures have been associated with higher injury severity and younger age, particularly under the age of 2 years [16–19]. In contrast, prior video-EEG monitoring series have demonstrated nonepileptic events in 15–43% of children in non-TBI populations, most frequently diagnosed in adolescence [20–26]. We hypothesized that our cohort would demonstrate a high rate of nonepileptic events, and that, furthermore, the "spells"

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Table 1
Cohort demographics.

		Cohort 1 (n = 116) (2002–2005)	Cohort 2 (n = 178) (2005–2010)	p-Value
Children with spells, n (%)		38 (33%)	34 (19%)	
% Female		37%	38%	0.90 (chi-square)
Injury severity, n (%)	Mild	23 (60%)	11 (32%)	0.04 (Fisher's exact)
	Moderate	3 (8%)	8 (24%)	
	Severe	12 (32%)	15 (44%)	
Age at injury (yrs)	Average	7.0	8.8	0.22 (*t*-test)
	SD	5.8	6.4	

would follow similar patterns to non-TBI populations, with epileptic seizures associated with higher injury severity and younger age of injury, and behavioral and other nonepileptic events associated with milder severity and older injury age.

2. Methods

Seizure-like phenomena were assessed through a single center analysis of paroxysmal events evaluated in children with a history of TBI. Subjects were drawn from two previously established databases of children evaluated at the UCLA Pediatric TBI center, all of whom were either acutely treated for their head injury at our hospital or evaluated in the outpatient Pediatric TBI clinic for the sequelae of prior TBI.

The first of the preexisting pediatric TBI databases was retrospectively collected and includes 116 children evaluated from 2002 to 2005. Because recruitment efforts occurred primarily in the outpatient setting, milder injuries were prominently represented, with 55% mild, 23% moderate, and 23% severe TBI cases. Injury severity was determined primarily by Glasgow Coma Scale (GCS) rating, with mild TBI generally associated with GCS of 13–15, moderate TBI with GCS between 8 and 13, and severe TBI with GCS $<$ 8. Per convention at our institution, children with GCS $\geq$ 13 with intracranial hemorrhage or skull fracture found on neuroimaging were classified as having suffered moderate TBI.

The second database consisted of 178 children who were prospectively enrolled between 2005 and 2010. This cohort was recruited both in the pediatric TBI clinic setting and during hospital admission for the treatment of head trauma, resulting in a larger proportion of children with more severe injuries: namely 36% mild, 39% moderate, and 25% severe TBI cases. Four children who had been enrolled in both databases were excluded from the earlier cohort and considered only with the 2005–2010 patients.

Both database studies were approved by the UCLA Institutional Review Board. Informed consent was obtained from the families of all patients prior to inclusion in the 2005–2010 TBI database.

3. Procedures

3.1. Cohort selection

Within each of these databases, the subset of children reported to have events suspicious for epileptic seizures or spells of an uncertain nature was included for analysis. Exclusion criteria included children suffering solely from impact seizures or other early posttraumatic seizures confined to the first week following TBI, as well as children whose spells lacked any clinical concern for epileptic seizures, such as syncope or postconcussive migraines, for which the diagnosis was clearly identified from the outset. Spell semiology, neuroimaging and electroencephalography (EEG) results, clinical diagnosis, and supplementary demographic information were obtained from the TBI databases and medical record review.

3.2. Classification of spell types

For each cohort subset, the spells were classified into five different categories based on the evaluation and assessment documented in the medical record: 1) PTE; 2) Epilepsy with other potential etiologies than TBI (e.g., clinical and/or EEG features suggestive of primary generalized or benign rolandic epilepsy, malformations of cortical development detected on neuroimaging); 3) Psychopathology (e.g., panic attacks); 4) Behavioral episodes (e.g., temper tantrums, attentional lapses) misinterpreted as seizures; and 5) Other neurologic events (e.g., sleep myoclonus, posturing, dysautonomia, postconcussive symptoms).

3.3. Statistical analysis

All analyses were performed using R version 2.12.1 (R Development Core Team, 2011, Vienna, Austria). Categorical demographic data, such as spell classification, injury severity, and gender, were analyzed using chi-square analyses or Fisher's exact tests when some fields had values $\leq$ 5. Differences in age at the time of injury were compared using two-tailed *t*-tests. p-Values $<$ 0.05 were considered statistically significant.

4. Results

4.1. Cohort subset comparison

The 2002–2005 database (Cohort 1) included 38 children with spells (Table 1). Four children had spells of two types: two with psychopathology and other neurologic events and two with misinterpreted behavior and PTE. The 2005–2010 database (Cohort 2) contained 34 children with spells. Seven children had more than one spell type: four with a combination of PTE and other neurologic events, one with misinterpreted behavior and other neurologic events, one with PTE and misinterpreted behavior, and one with psychopathology and other neurologic events. Among children suffering from paroxysmal spells, Cohort 1 had a larger representation of mild TBI (60% vs. 32%), whereas Cohort 2 had more children with moderate TBI (8% vs. 24%). Gender distribution and average age at the time of injury were not significantly different (Table 1). The proportion of children was also similar between the two subsets for all spell classifications (Table 2).

4.2. Combined cohort analyses

Due to the similarities between Cohorts 1 and 2, the results were combined for further analyses (Fig. 1). This combined cohort consisted of 72 children with paroxysmal spells: 34 with history of mild TBI, 11 with moderate TBI, and 27 with severe TBI. Eighty-four

Table 2
Distribution of spell classification by cohort.

	Posttraumatic epilepsy	Epilepsy, other etiologies	Psychopathology	Misinterpreted behavior	Other neurologic events
Cohort 1 (2002–2005)	18	8	7	3	7
Cohort 2 (2005–2008)	14	3	7	5	12
p-Value	0.77	0.20	0.95	0.46	0.18

Evaluated by chi-square or Fisher's exact test.