Published in final edited form as:
J Pediatr. 2014 February ; 164(2): 339–346.e2. doi:10.1016/j.jpeds.2013.09.032.

Electrographic seizures after convulsive status epilepticus in children and young adults. A retrospective multicenter study

Iván Sánchez Fernández, MD[1,2], **Nicholas S. Abend, MD**[3], **Daniel H. Arndt, MD**[4], **Jessica L. Carpenter, MD**[5], **Kevin E Chapman, MD**[6], **Karen M. Cornett, BS, MT**[7], **Dennis J. Dlugos, MD**[3], **William B. Gallentine, DO**[7], **Christopher C Giza, MD**[8], **Joshua L Goldstein, MD**[9], **Cecil D Hahn, MD, MPH**[10], **Jason T Lerner, MD**[8], **Joyce H Matsumoto, MD**[8], **Kristin McBain, MS**[10], **Kendall B Nash, MD**[11], **Eric Payne, MD**[10], **Sarah M Sánchez, BA**[3], **Korwyn Williams, MD, PhD**[12], and **Tobias Loddenkemper, MD**[1]

[1]Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA

[2]Department of Child Neurology, Hospital Sant Joan de Déu, Universidad de Barcelona, Barcelona, Spain

[3]Departments of Neurology and Pediatrics, The Children's Hospital of Philadelphia and the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

[4]Departments of Pediatrics and Neurology, Oakland University William Beaumont School of Medicine, Royal Oak, MI

[5]Department of Neurology, Children's National Medical Center, Washington DC

[6]Division of Neurology, Children's Hospital Colorado and University of Colorado School of Medicine, Aurora, CO

[7]Division of Pediatric Neurology, Duke University Hospital and Duke University School of Medicine, Durham, NC

[8]Division of Neurology, Department of Pediatrics Mattel Children's Hospital and UCLA Brain Injury Research Center, Department of Neurosurgery, David Geffen School of Medicine at UCLA, Los Angeles, CA

[9]Division of Neurology, Children's Memorial Hospital and Northwestern University Feinberg School of Medicine, Chicago, IL

[10]Division of Neurology, The Hospital for Sick Children and University of Toronto, Toronto, ON

[11]Department of Neurology, University of California San Francisco, San Francisco, CA

[12]Department of Pediatrics, University of Arizona College of Medicine and Barrow's Neurological Institute at Phoenix Children's Hospital, Phoenix, AZ

Abstract

Correspondence: Nicholas Abend, MD, The Children's Hospital of Philadelphia, Division of Neurology, The Perelman School of Medicine at the University of Pennsylvania, 3501 Civic Center Boulevard, Philadelphia, Pennsylvania, PA, 19104, Phone: 215-590-1719. Fax: 215-590-1771, abend@email.chop.edu.
Funding information and conflicts of interest are available at www.jpeds.com (Appendix).

Objectives—To describe the prevalence, characteristics and predictors of electrographic seizures following convulsive status epilepticus (CSE).

Study design—Multicenter retrospective study describing clinical and electroencephalographic (EEG) features of children (1 month-21 years) with CSE who underwent continuous EEG monitoring.

Results—Ninety-eight children (53 males) with a median age of 5 years with CSE underwent subsequent continuous EEG monitoring after CSE. Electrographic seizures (with or without clinical correlate) were identified in 32 subjects (33%). Eleven subjects (34.4%) had electrographic-only seizures, 17 subjects (53.1%) had electro-clinical seizures, and 4 subjects (12.5%) had an unknown clinical correlate. Of the 32 subjects with electrographic seizures, 15 subjects (46.9%) had electrographic status epilepticus. Factors associated with the occurrence of electrographic seizures after CSE were a prior diagnosis of epilepsy (p= 0.029) and the presence of interictal epileptiform discharges (p< 0.0005). The median (p_{25}–p_{75}) duration of stay in the pediatric intensive care unit was longer for children with electrographic seizures than for children without electrographic seizures [9.5 (3–22.5) versus 2 (2–5) days, Wilcoxon test, Z=3.916, p=0.0001]. Four children (4.1%) died before leaving the hospital and we could not identify a relationship between death and the presence or absence of electrographic seizures.

Conclusions—Following CSE, one-third of children who underwent EEG monitoring experienced electrographic seizures, and among these, one-third experienced entirely electrographic-only seizures. A prior diagnosis of epilepsy and the presence of interictal epileptiform discharges were risk factors for electrographic seizures.

Keywords

Critical Care; Continuous monitoring; Electroencephalogram; Intensive Care Unit; Pediatric

Status epilepticus is a common pediatric neurologic emergency (1). It is a life-threatening condition with a mortality rate of approximately 1–3% in the pediatric population (2–5). Additionally, surviving children may experience lifelong sequelae including cognitive and neurodevelopmental impairments, epilepsy, and recurrent status epilepticus (2,6).

Management has long focused on aggressive treatment of convulsive seizures. However, there is increasing recognition that electrographic-only seizures can persist after convulsive seizures are terminated. Electrographic (EEG) seizures refer to an abnormal EEG pattern that could be accompanied by a clinical correlate (electro-clinical seizures) or not associated with any clinical change (electrographic-only seizures). The terms “subclinical” and “non-convulsive” seizures have been variably used to refer to electrographic-only seizures or seizures with only subtle manifestations. A recent Neurocritical Care Society guideline considered convulsive and electrographic-only seizures as needing equivalently aggressive management and recommended that the “treatment of status epilepticus should occur rapidly and continue sequentially until electrographic seizures are halted” (7). In order to identify electrographic seizures, the guideline recommended that “continuous electroencephalographic monitoring should be initiated within one hour of status epilepticus onset if ongoing seizures are suspected”. Although these recommendations are strong, the guideline acknowledges that only low quality data support the recommendation (7) because the occurrence of electrographic seizures following control of CSE has not been specifically studied in children (Table I; available at www.jpeds.com). Several studies focused on EEG monitoring have described the occurrence of electrographic seizures among children who presented with CSE, but this was not the central focus of the research and the CSE cohorts were small. Slightly more data are available in adults. In a prospective single-center series, 79 of 164 adults (48%) developed electrographic-only seizures after control of CSE (13).

The objective of this multi-center, retrospective study was to begin to address the knowledge gap between EEG monitoring recommendations (7) and supporting data. We aimed to: 1) determine the proportion of children who experience electrographic seizures after resolution of CSE, 2) describe the characteristics of electrographic seizures and EEG patterns following CSE, and 3) identify predictors of electrographic seizure occurrence.

METHODS

This was a retrospective, descriptive, multi-center study. This study was carried out by 11 pediatric institutions that are members of the Pediatric Critical Care EEG Group (PCCEG) which is the pediatric component of the Critical Care EEG Monitoring Consortium (CCEMRC). The study protocol was approved by the Institutional Review Board at each site and included waived consent given the retrospective nature of the study.

Each of the 11 centers provided data for 50 consecutive children aged 1 month to 21 years who underwent clinically indicated continuous EEG monitoring in the pediatric intensive care unit. Information on the complete cohort of 550 critically ill children can be found elsewhere (14,15). This study focuses on the subset of children who experienced CSE prior to continuous EEG monitoring.

EEG monitoring was performed using the international 10–20 system of electrode placement and the standard EEG system at each institution. All institutions had EEG monitoring available and in regular use in the critical care setting. All centers used simultaneous video recording. Decisions on whether and when to start continuous EEG monitoring, and the duration of the continuous EEG monitoring were taken by the individual clinicians based on best expected clinical utility for each individual patient. If there were multiple EEG monitoring sessions during the same admission then only data from the first session was included. EEG monitoring interruptions lasting less than 12 hours were considered the same session.

These included age, sex, prior neurologic diagnoses (including diagnoses of epilepsy, epileptic encephalopathy, developmental delay/intellectual disability, and other neurologic diagnoses), acute neurologic disorder, mental status at the onset of EEG monitoring, duration of stay in the pediatric intensive care unit, and in-hospital mortality. Acute neurologic disorders were grouped into three categories: (1) epilepsy-related, (2) acute structural (stroke, central nervous system inflammation or autoimmune disorder, traumatic brain injury, central nervous system infection, brain malformation, tumor/oncologic, and hypoxic-ischemic encephalopathy), and (3) acute non-structural (sepsis, metabolic, pharmacologic sedation, toxin, paralytic administration). Because of insufficient information on timing in clinical charts, the timing of EEG monitoring relative to the beginning of the CSE was not specified.

These included electrographic seizure occurrence and characteristics, initial and typical EEG background category, and occurrence of interictal epileptiform discharges. Electrographic seizures were defined as abnormal, paroxysmal EEG events that were different from the background, lasted longer than ten seconds (or shorter if associated with a clinical seizure), had a plausible EEG field, and evolved in morphology and spatial distribution. Electrographic seizures were classified as electrographic status epilepticus if any single seizure lasted longer than 30 minutes (continuous electrographic status epilepticus) or if recurrent seizures together lasted for more than 30 minutes in any one hour epoch (50% seizure burden) (intermittent electrographic status epilepticus). The threshold for diagnosing CSE has been progressively changed from 30 minutes to 5 minutes (16–18). However, the threshold for defining electrographic status epilepticus is less clear. We used a 30 minute

definition because prior studies utilizing this definition have reported that it distinguished between: a) electrographic seizures not associated with short-term mortality or worsening neurologic outcome and b) electrographic status epilepticus which was associated with short-term mortality and worse neurologic outcome (14, 19).

Electrographic seizure characteristics included typical duration, and anatomical localization at seizure onset and maximal extent. Electrographic seizures were also classified as electrographic-only seizures if none of the seizures had a clinical correlate or electro-clinical seizures if at least some of the seizures had a clinical correlate. Electro-clinical seizures were subdivided based on the proportion of electrographic seizures with a clinical correlate: some (1–49%), most (50–99%), or all (100%).

Data were collected and managed using REDCap (Research Electronic Data Capture) hosted at The Children's Hospital of Philadelphia Research Institute. REDCap is a secure, web-based application designed to support data capture for research studies using an intuitive data entry interface, audit trails, and export procedures to download to common statistical packages (20).

Statistical analyses

Descriptive statistics are presented as medians and p_{25}–p_{75} ranges for continuous variables and as counts and percentages for categorical variables. We evaluated potential risk factors for electrographic seizure occurrence using the chi-squared test for categorical variables and the Wilcoxon rank-sum (Mann-Whitney) test for continuous variables. Further multivariable analysis was not performed because only two variables predicted electrographic seizure occurrence. All statistics were performed using STATA (Version 12.0, STATA Corp, Texas, USA).

RESULTS

Ninety-eight children (53 males) with a median age of 5 years underwent EEG monitoring following CSE and constituted our study cohort. Three out of the 98 patients were 18 years or older. The main demographic and etiological features are presented in Table II.

The most frequent indication for continuous EEG monitoring was the presence of encephalopathy with possible electrographic seizures followed by management of refractory status epilepticus. The duration and main characteristics of EEG monitoring are presented in Table III.

Electrographic seizures occurred in 32 of 98 subjects (32.7%) following CSE. Among the 32 subjects with electrographic seizures, 17 subjects (53.1%) had some clinical correlate and thus might have been identified by close clinical observation, 11 subjects (34.4%) had electrographic-only seizures and thus would not have been identified without EEG monitoring, and 4 subjects (12.5%) did not have data about clinical correlate, despite continuous video monitoring during the events. Of the 32 with electrographic seizures, 15 subjects (46.9%) had electrographic status epilepticus which was characterized as continuous electrographic status epilepticus in 6 subjects (40%) and intermittent electrographic status epilepticus in 9 subjects (60%). Seven of the 15 subjects (46.7%) with electrographic status epilepticus had electrographic-only seizures which would not have been identified without EEG monitoring. Two of 19 subjects (10.5%) diagnosed with febrile convulsive status epilepticus had subsequent electrographic seizures. The main characteristics of the electrographic seizures are presented in Table IV.

We evaluated potential predictors of electrographic seizure occurrence using univariate analysis. Table II presents univariate analyses for clinical variables and Table III presents univariate analyses for EEG variables. The presence of a prior diagnosis of epilepsy (Table II) and the occurrence of interictal epileptiform discharges (Table III) were associated with electrographic seizures. Subjects with electrographic seizures had a longer duration of EEG monitoring and a higher frequency of burst-suppression in the typical EEG background (Table III).

When comparing subjects with electrographic status epilepticus to subjects without electrographic status epilepticus (no electrographic seizures, or electrographic seizures but not electrographic status epilepticus) the presence of an abnormal initial EEG background category (Pearson chi-square= 9.7346, p= 0.045) and the presence of interictal epileptiform discharges (Pearson chi-square= 11.7072, p= 0.001) were associated with electrographic status epilepticus. Age, the presence of prior developmental delay or intellectual disability, acute neurologic disorder, mental status at the beginning of the EEG monitoring, and the presence of a prior diagnosis of epilepsy did not predict the occurrence of electrographic status epilepticus.

Patients experiencing some seizures with a clinical correlate might be identified by close observation, and patients with exclusively electrographic-only seizures could not be identified without EEG monitoring. Thus, we analyzed the dataset for predictors of electrographic-only seizures by comparing the 11 subjects with electrographic-only seizures to the 17 subjects with electro-clinical seizures. Age (Wilcoxon rank-sum (Mann-Whitney) test z= −1.176, p= 0.2395), the presence of a prior developmental delay or intellectual disability (Pearson Chi-square= 0.4492, p= 0.503), acute neurologic disorder (Pearson Chi-square= 1.9874, p= 0.370), mental status at the beginning of the continuous EEG monitoring (Pearson Chi-square= 1.4392, p= 0.487), initial EEG background category (Pearson Chisquare= 1.8201, p= 0.769), the presence of a prior diagnosis of epilepsy (Pearson Chi-square= 2.4456, p= 0.118), and the presence of interictal epileptiform discharges (Pearson Chi-square= 0.0499, p= 0.823) did not predict the occurrence of electrographic-only seizures.

Four out of 98 patients (4.1%) died before hospital discharge. We evaluated potential predictors of mortality using univariate analysis. No differences in mortality were found when comparing children with or without electrographic seizures (Table II).

We evaluated potential predictors of intensive care unit length of stay using univariate analysis. Children with electrographic seizures had a median (p_{25}–p_{75}) duration of stay in the pediatric intensive care unit [9.5 (3–22.5) days] that was longer than that of children without electrographic seizures [2 (2–5) days] (Wilcoxon test, Z=3.916, p=0.0001). Children with electrographic status epilepticus had a median (interquartile range) duration of stay in the pediatric intensive care unit [21 (9–49) days] that was significantly longer than that of children with electrographic seizures without electrographic status epilepticus [3 (2–10) days] (Wilcoxon test, Z=3.389, p= 0.0007). When comparing children with electrographic-only seizures and children with electro-clinical seizures, we could not find differences in the duration of stay in the pediatric intensive care unit (Wilcoxon test, Z=1.344, p=0.179).

DISCUSSION

Approximately one third of children with CSE, who underwent clinically indicated EEG monitoring experienced subsequent electrographic seizures. Additionally, one third of children with electrographic seizures (approximately 11% of the total children with monitoring after CSE) experienced exclusive electrographic-only seizures which could not

have been identified without EEG monitoring. On univariate analysis, factors associated with the development of electrographic seizures after CSE were prior diagnosis of epilepsy and the presence of interictal epileptiform discharges. The presence of an abnormal EEG background at the beginning of the monitoring session and the presence of interictal epileptiform activity were associated with electrographic status epilepticus. The occurrence of electrographic seizures was associated with a longer stay in the pediatric intensive care unit.

The demographic characteristics of our population are similar to those of other series of children with convulsive status epilepticus (3,9,10,12,21–26) with some etiology differences depending on whether studies were performed in an intensive care unit setting or in an ambulatory setting.

Although recent guidelines advocate for the use of EEG monitoring after CSE (7), the frequency of electrographic seizures following CSE has not been previously studied in children. The most similar series to ours was performed in 164 adults (age ≥16y) who underwent EEG monitoring following control of CSE (13). Electrographic-only seizures occurred in 79 subjects (48%), including 23 subjects (14%) with non-convulsive status epilepticus (13). Similar data in children can only be roughly estimated based on the scarce indirect information available. In two small retrospective case series of children with non-convulsive status epilepticus, there was preceding CSE in 5 of 19 children (26%) (8) and in 4 of 7 children (57%) (9). A different study found that electrographic seizures occurred in 29 of 56 patients (52%) who had prior convulsive seizures (without specifics regarding which proportion had CSE) (11). In a large pediatric study of 122 children who underwent EEG monitoring, the likelihood of experiencing an electrographic seizure was five times higher if the underlying diagnosis was prior clinical status epilepticus (10). Our data provide an estimate of the prevalence of electrographic seizures following CSE in a larger multi-center cohort and we studied this aspect prospectively: from CSE to electrographic seizures.

We identified prior diagnosis of epilepsy and the presence of interictal epileptiform discharges as risk factors for electrographic seizures after CSE. Any comparisons with previous studies are limited because other series of children undergoing EEG monitoring assessed for electrographic seizure risk factors in broader cohorts, and not only in children with CSE. Factors that have been associated with electrographic seizure occurrence in these cohorts included an acute presentation of epilepsy, acute structural neurologic etiology, acute non-structural neurologic etiology, prior diagnosis of epilepsy, and epileptiform discharges on EEG (12); coma, age<18y, history of epilepsy, and convulsive seizures during the current illness (22); young age (11); age younger than two years and clinical seizures prior to EEG monitoring (21). Although predictors are heterogeneous in these different studies, the presence of prior seizures or epileptiform activity and younger age were consistently associated with an increased risk of electrographic seizures. In our series, epilepsy and epileptiform activity were associated with electrographic seizure occurrence, but age was not associated with electrographic seizures. By identifying risk factors for electrographic seizures our study may help target limited EEG monitoring resources to children most at risk for experiencing electrographic seizures.

The principal goal of treatment in status epilepticus is to stop both clinical and electrographic seizures as soon as possible (7), but the clinical impact of EEG monitoring and electrographic seizure identification remains unclear. In one study of critically ill neonates and children, electrographic seizure occurrence was associated with an unfavorable outcome (27). In two studies of critically ill children, the occurrence of electrographic status epilepticus but not electrographic seizures was associated with higher mortality (14,19) and worse short-term outcome (19). Physiologic mechanisms that could lead to worse outcome

have been identified. Specifically, non-convulsive seizures have been associated with increased intracranial pressure and a higher lactate/pyruvate ratio in adults with traumatic brain injury (28). Presumably, identification of electrographic seizures by EEG monitoring results in at least partially effective treatment and exposure to a lower seizure burden, although this has only been demonstrated in neonates. In a prospective study, neonates underwent amplitude integrated EEG monitoring and were randomized to permit or restrict physician access to amplitude integrated EEG data. When physicians had access to amplitude integrated EEG data and could modify management based on these data, neonates experienced a tendency towards lower seizure duration, lower brain injury evident on magnetic resonance imaging, and lower mortality (29). Observational studies have reported that EEG monitoring results in anticonvulsant changes in about one-half of critically ill children and adults who undergo EEG monitoring (30,31) and that seizures can often be terminated with existing antiseizure medications (32). Further study is needed to establish whether these anticonvulsant changes result in reduced seizure exposure or in a change in outcome.

The 4% mortality in this cohort is slightly higher than the range of mortalities found in prior pediatric series of CSE of approximately 1–3% (2–5), possibly reflecting the more severe cases cared for in the pediatric intensive care units who were chosen to undergo EEG monitoring. In the adult series, the mortality of patients with non-convulsive status epilepticus and with interictal discharges after CSE was higher than in patients without interictal discharges after CSE (13). We could not find evidence that the presence or absence of electrographic seizures influenced mortality in our series. The etiology of CSE is a major determinant of mortality (3,6,33), but we could not replicate those findings in our series. Very limited in-hospital mortality in our series may account for the lack of statistically significant differences. However, we found that presence of electrographic seizures and presence of electrographic status epilepticus were associated with a longer stay in the intensive care unit.

This study needs to be interpreted in the clinical setting of data acquisition including the possibility of information and selection bias. First, continuous EEG monitoring was not initiated as part of a prospective protocol with pre-specified criteria. Rather, the decision to monitor patients was based on clinical judgments and on a case by case basis. This may have resulted in an overestimation of the electrographic seizure prevalence by selecting seizure-prone cases. On the other hand, we may have underestimated the overall electrographic seizure prevalence because some patients with electrographic seizures may not have been monitored. Timing of EEG monitoring relative to the beginning of the status epilepticus was not captured and this factor may add to an over- or under-estimation of the real frequency of electrographic seizures after CSE. The clinical correlate of four patients with electrographic seizures was unknown because of the retrospective nature of our study. Although imperfect, these data indicate that sufficient numbers of children may experience electrographic status epilepticus following CSE to justify continuous EEG monitoring in this population and therefore warrant further prospective study. Second, we applied standard definitions for electrographic seizures and status epilepticus to limit information bias and all EEG interpretations were performed by pediatric neurophysiologists, but we did not utilize multi-reader scoring and thus could not confirm the level of inter-rater agreement. Additionally, electrographic status epilepticus represented a combined outcome involving both long electrographic seizures and recurrent electrographic seizures adding to heterogeneity. Finally, the only outcome measures assessed were mortality and pediatric intensive care unit length of stay. Neither electrographic seizures nor electrographic status epilepticus were associated with higher mortality, but our numbers were small. Also, more detailed outcome measures related to neurocognitive status may be more sensitive to seizure-induced injury. Importantly, because EEG monitoring was clinically indicated the findings were acted upon

by clinicians. Most centers target electrographic seizures for treatment if identified. Thus, mortality might have been higher among subjects with electrographic seizures or electrographic status epilepticus had they not been targeted for management and thus their seizures would have presumably persisted longer. Our study collected the variable of electrographic seizures as a dichotomous variable: present/absent. Therefore, we are not able to answer the interesting question of whether the higher yield of capturing electrographic seizures in the group with >72 hours of monitoring was secondary to a long monitoring or because monitoring was continued because of prior detection of electrographic seizures. This will be subject of future studies with more detailed EEG screening as the yield of electrographic seizure detection when comparing the different durations of EEG timing would provide valuable clinical guidance to clinicians. Some of these challenges could be overcome by a prospective study which involves prospective screening of all patients with CSE for specific EEG monitoring indications, multi-reader EEG scoring, more detailed seizure burden measurement, and more detailed outcome assessments. Our finding that electrographic seizures are common in this population suggests that such prospective studies are warranted.

Further study is needed to establish whether electrographic seizures are an epiphenomenon and simply reflect brain injury or whether they cause neuronal injury and worsen outcome. Additionally, it is not known whether management of electrographic seizures leads to improved outcomes. The present study sets the stage for future prospective studies that will evaluate whether modification of electrographic seizures with antiseizure medications modifies the outcome in these patients.

Abbreviations

EEG	Electroencephalogram (or elecetroencephalographic)
CSE	Convulsive status epilepticus
PCCEG	Pediatric Critical Care Electroencephalogram Group
REDCap	Research Electronic Data Capture

REFERENCES

1. Loddenkemper T, Goodkin HP. Treatment of pediatric status epilepticus. Curr treat opt neurol. 2011; 13:560–573.
2. Maytal J, Shinnar S, Moshé SL, Alvarez LA, Shinnar S, Mosh SL. Low Morbidity and Mortality of Status Epilepticus in Children. Pediatrics. 1989; 83:323–331. [PubMed: 2919138]
3. Chin RFM, Neville BGR, Peckham C, Bedford H, Wade A, Scott RC. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. Lancet. 2006; 368:222–229. [PubMed: 16844492]
4. DeLorenzo RJ, Hauser Wa, Towne aR, Boggs JG, Pellock JM, Penberthy L, et al. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. Neurology. 1996; 46:1029–1035. [PubMed: 8780085]
5. Loddenkemper T, Syed TU, Ramgopal S, Gulati D, Thanaviratananich S, Kothare SV, et al. Risk factors associated with death in in-hospital pediatric convulsive status epilepticus. PloS one. 2012; 7:e47474. [PubMed: 23110074]
6. Barnard C, Wirrell E. Does Status Epilepticus in Children Cause Developmental Deterioration and Exacerbation of Epilepsy? J Child Neurol. 1999; 14:787–794. [PubMed: 10614565]
7. Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, et al. Guidelines for the evaluation and management of status epilepticus. Neurocritical care. 2012; 17:3–23. [PubMed: 22528274]

8. Tay SKH, Hirsch LJ, Leary L, Jette N, Wittman J, Akman CI. Nonconvulsive status epilepticus in children: clinical and EEG characteristics. Epilepsia. 2006; 47:1504–1509. [PubMed: 16981867]
9. Shahwan A, Bailey C, Shekerdemian L, Harvey aS. The prevalence of seizures in comatose children in the pediatric intensive care unit: a prospective video-EEG study. Epilepsia. 2010; 51:1198–1204. [PubMed: 20163439]
10. Williams K, Jarrar R, Buchhalter J. Continuous video-EEG monitoring in pediatric intensive care units. Epilepsia. 2011; 52:1130–1136. [PubMed: 21671924]
11. Abend NS, Gutierrez-Colina aM, Topjian aa, Zhao H, Guo R, Donnelly M, et al. Nonconvulsive seizures are common in critically ill children. Neurology. 2011; 76:1071–1077. [PubMed: 21307352]
12. McCoy B, Sharma R, Ochi A, Go C, Otsubo H, Hutchison JS, et al. Predictors of nonconvulsive seizures among critically ill children. Epilepsia. 2011; 52:1973–1978. [PubMed: 22003955]
13. DeLorenzo RJ, Waterhouse EJ, Towne aR, Boggs JG, Ko D, DeLorenzo Ga, et al. Persistent nonconvulsive status epilepticus after the control of convulsive status epilepticus. Epilepsia. 1998; 39:833–840. [PubMed: 9701373]
14. Abend NS, Arndt DH, Carpenter JL, Chapman KE, Cornett KM, Gallentine WB, et al. Electrographic Seizures in Pediatric ICU Patients: A Cohort Study of Risk Factors and Mortality. Neurology. 2013; 81:383–391. [PubMed: 23794680]
15. Sánchez SM, Arndt DH, Carpenter JL, Chapman KE, Cornett KM, Dlugos DJ, et al. Electroencephalographic Monitoring in Critically Ill Children: Current Practice and Implications for Future Study Design. Epilepsia. 2013; 54:1419–1427. [PubMed: 23848569]
16. Brodie MJ. Status epilepticus in adults. Lancet. 1990; 336:551–552. [PubMed: 1975048]
17. Lowenstein DH, Bleck T, Macdonald RL. It's time to revise the definition of status epilepticus. Epilepsia. 1999; 40:120–122. [PubMed: 9924914]
18. Brophy GM, Bell R, Claassen J, Alldredge B, Bleck TP, Glauser T, et al. Guidelines for the evaluation and management of status epilepticus. Neurocrit care. 2012; 17:3–23. [PubMed: 22528274]
19. Topjian, Aa; Gutierrez-Colina, AM.; Sanchez, SM.; Berg, Ra; Friess, SH.; Dlugos, DJ., et al. Electrographic status epilepticus is associated with mortality and worse short-term outcome in critically ill children. Criti Care Med. 2013; 41:215–223.
20. Harris, Pa; Taylor, R.; Thielke, R.; Payne, J.; Gonzalez, N.; Conde, JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009; 42:377–381. [PubMed: 18929686]
21. Schreiber JM, Zelleke T, Gaillard WD, Kaulas H, Dean N, Carpenter JL. Continuous video EEG for patients with acute encephalopathy in a pediatric intensive care unit. Neurocrit Care. 2012; 17:31–38. [PubMed: 22565632]
22. Claassen J, Mayer Sa, Kowalski RG, Emerson RG, Hirsch LJ. Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. Neurology. 2004; 62:1743–1748. [PubMed: 15159471]
23. Saengpattrachai M, Sharma R, Hunjan A, Shroff M, Ochi A, Otsubo H, et al. Nonconvulsive seizures in the pediatric intensive care unit: etiology, EEG, and brain imaging findings. Epilepsia. 2006; 47:1510–1518. [PubMed: 16981868]
24. Hyllienmark L, Amark P. Continuous EEG monitoring in a paediatric intensive care unit. Eur J Paediatr Neurol. 2007; 11:70–75. [PubMed: 17188917]
25. Shinnar S, Pellock JM, Moshé SL, Maytal J, O'Dell C, Driscoll SM, et al. In whom does status epilepticus occur: age-related differences in children. Epilepsia. 1997; 38:907–914. [PubMed: 9579892]
26. Waterhouse EJ, Garnett LK, Towne aR, Morton LD, Barnes T, Ko D, et al. Prospective population-based study of intermittent and continuous convulsive status epilepticus in Richmond, Virginia. Epilepsia. 1999; 40:752–758. [PubMed: 10368074]
27. Kirkham FJ, Wade AM, McElduff F, Boyd SG, Tasker RC, Edwards M, et al. Seizures in 204 comatose children: incidence and outcome. Intensive Care Med. 2012; 38:853–862. [PubMed: 22491938]

28. Vespa PM, Miller C, McArthur D, Eliseo M, Etchepare M, Hirt D, et al. Nonconvulsive electrographic seizures after traumatic brain injury result in a delayed, prolonged increase in intracranial pressure and metabolic crisis. Crit Care Med. 2007; 35:2830–2836. [PubMed: 18074483]

29. Van Rooij LGM, Toet MC, Van Huffelen AC, Groenendaal F, Laan W, Zecic A, et al. Effect of treatment of subclinical neonatal seizures detected with aEEG: randomized, controlled trial. Pediatrics. 2010; 125:e358–e366. [PubMed: 20100767]

30. Abend NS, Topjian Aa, Gutierrez-Colina AM, Donnelly M, Clancy RR, Dlugos DJ. Impact of continuous EEG monitoring on clinical management in critically ill children. Neurocrit Care. 2011; 15:70–75. [PubMed: 20499208]

31. Kilbride RD, Costello DJ, Chiappa KH. How seizure detection by continuous electroencephalographic monitoring affects the prescribing of antiepileptic medications. Arch Neurol. 2009; 66:723–728. [PubMed: 19506131]

32. Abend NS, Sanchez SM, Berg Ra, Dlugos DJ, Topjian Aa. Treatment of electrographic seizures and status epilepticus in critically ill children: A single center experience. Seizure. 2013; 22:467–471. [PubMed: 23601851]

33. Logroscino G, Hesdorffer DC, Cascino G, Annegers JF, Hauser Wa. Short-term mortality after a first episode of status epilepticus. Epilepsia. 1997; 38:1344–1349. [PubMed: 9578531]

Appendix

I.S.F is funded by a grant for the study of Epileptic Encephalopathies from “Fundación Alfonso Martín Escudero”. N.A. is funded by the National Institutes of Health (NIH; K23NS076550) and the Children’s Hospital of Philadelphia Department of Pediatrics, and receives royalties from Demos Medical Publishing. D.A. is on the speaker’s bureau for Cyberonics. D.D. is funded by NIH (1R01NS053998, 2U01NS045911, 1R01LM011124, and U01NS077276), and has also given expert testimony in medico-legal cases. C.G. is supported by National Institute of Neurological Disorders and Stroke (NINDS), Thrasher Research Foundation, Child Neurology Foundation/Winokur Family Foundation, Today’s and Tomorrow’s Children’s Fund, University of California, Los Angeles, Grants Program, and National Football League Charities. C.H. receives research funding from the Canadian Institutes of Health Research, the PSI Foundation, and the SickKids Foundation. T.L. serves on the Laboratory Accreditation Board for Long Term (Epilepsy and ICU) Monitoring, serves as a member of the American Clinical Neurophysiology Council, serves on the American Board of Clinical Neurophysiology, serves as an Associate Editor for *Seizure* (the European Journal of Epilepsy), performs and receives payments for video EEG longterm monitoring, EEGs, and other electrophysiological studies at Boston Children's Hospital, receives support from NIH/NINDS (1R21NS076859-01 [2011–2013]), is supported by a Career Development Fellowship Award from Harvard Medical School and Boston Children's Hospital, by the Program for Quality and Safety at Boston Children's Hospital, by the Payer Provider Quality Initiative, receives funding from the Epilepsy Foundation of America (EF-213583 and EF-213882), from the Center for Integration of Medicine & Innovative Technology (CIMIT), the Translational Research Project at Boston Children’s Hospital, the Epilepsy Therapy Project, by an Infrastructure Award from American Epilepsy Society, Cure, and received investigator initiated research support from Eisai Inc and Lundbeck. The other authors declare no conflicts of interest. The sponsors did not participate in study design, data collection, analysis and interpretation, writing of the manuscript, or the decision to submit the manuscript for publication.

J Pediatr. Author manuscript; available in PMC 2015 February 01.

Table 1

Summary of relevant literature related to the present work.

Author and year	Number of patients	Characteristics of the study	Patient population	Nonconvulsive seizures	Relationship of nonconvulsive seizures with convulsive status epilepticus
DeLorenzo et al, 1998 (13)	164 adult patients (≥16y)	Prospectivestudy.	Patients monitored with continuous EEG after resolution of convulsive status epilepticus.		79/164 (48% developed onconvulsive seizures [23/164 14% nonconvulsive status pilepticus] after resolution of onvulsive status epilepticus
McCoy et al, 2011 (12)	121 children (60% were <1y)	Retrospectivesudy.	Patients monitored with continuous EEG in the neonatal and pediatric intensive care units.	35/121 (29%) had nonconvulsive seizures Factors associated with nonconvulsive seizures: acute presentation of epilepsy, acute structural brain etiology, acute nonstructural brain etiology, prior diagnosis of epilepsy, and interictalepileptiform discharges on EEG	
Tay et al, 2006 (8)	19 children (1mo to 17 years)	Retrospective study.	Patients with nonconvulsive status epilepticus.		5/19 (26%) patients developed nonconvulsive status epilepticus after convulsive status epilepticus and 12/19 (63%) developed nonconvulsive status epilepticus after brief convulsions
Shahwan et al, 2010 (9)	100 children (2mo to 17y)	Prospective study.	Patients with depressed consciousness (Glasgow coma scale<8).	7/100 (7%) had nonconvulsive seizures	4/7 (57%) patients had convulsive status epilepticus before developing electrical seizures
Saengpatt rachai et al, 2006 (20)	141 pediatric patients (> 1mo)	Retrospective study.	Patients with depressed level of consciousness.	23/141 (16%) had nonconvulsive seizures	
Claassen et al, 2004 (19)	570 patients (75 patients<18y , 41 patients<2y)	Retrospective study.	Patients with continuous EEG monitoring.	101/570 (18%) had nonconvulsive seizures Factors associated with nonconvulsive seizures: coma, age<18y, history of epilepsy, and convulsive seizures during the current illness	
Abend et al, 2011 (11)	100 children (interquartile range 0.8 to 9.7y).	Prospective study.	Patients with acute encephalopathy and EEG monitoring.	46/100 (46%) had nonconvulsive seizures, 19/100 (19%) had nonconvulsive status epilepticus Factor associated with nonconvulsive seizure: young age	Electrographic seizures occurred in 29/56 (52%) of patients with convulsive seizures prior to EEG monitoring and in 17/44 (39%) of patients without convulsive seizures prior to EEG monitoring.
Schreiber et al, 2012 (18)	94 children (1mo to 18y)	Prospective study.	Patients with acute encephalopathy (Glasgow coma scale<12).	27/94 (29%) had nonconvulsive seizures, 17/94 (18%) had nonconvulsive status epilepticus Factors associated with nonconvulsive seizures: age<2y, and clinical seizures prior to EEG monitoring	
Williams et al, 2011 (10)	122 patients (2 days to 17y)	Retrospective study.	Patients with EEG monitoring in the neonatal and pediatric intensive care unit.	34/122 (28%) had nonconvulsive seizures	Factors associated with electrographic seizures: prior convulsive status epilepticus and epileptiformactivity[C1]

Table 2

Demographic and etiological characteristics in patients with and without electrographic seizures

Category	Total population (with and without electrographic seizures)		No electrographic seizures	Electrographic seizures	Difference
Age in years during the SE episode (years) (N=98)	Median (p25–p75)	5 (2–12.4)	4.3 (2.2–12.4)	6.3 (1.9–11.9)	WRS z= − 0.121 *p*= 0.9035
	Mean (SD)	6.9 (5.9)	6.9 (6.1)	7.1 (5.3)	
	Range	0.25–21	0.3–21	0.25–16	
Sex (N=98)	Male	53 (54.1%)	36 (54.6%)	17 (53.1%)	PCS= 0.0175 *p*= 0.895
	Female	45 (45.9%)	30 (45.5%)	15 (46.9%)	
Etiologic acute neurologic disorder (N=98)	Epilepsy related	60 (61.2%)	36 (54.6%)	24 (75%)	PCS= 4.3679 *p*= 0.113
	Acute symptomatic non-structural	24 (24.5%)	20 (30.3%)	4 (12.5%)	
	Acute symptomatic structural	14 (14.3%)	10 (15.2%)	4 (12.5%)	
Prior developmental delay/intellectual disability (N=98)	Yes	59 (60.2%)	37 (26.1%)	22 (68.8%)	PCS= 1.7552 *p*= 0.416
	No	38 (38.8%)	28 (42.4%)	10 (31.3%)	
	Unknown	1 (1%)	1 (1.5%)	0 (0%)	
Prior diagnosis of epilepsy (N=98)	Yes	56 (57.1%)	33 (50%)	23 (71.9%)	PCS= 7.0867 ***p*= 0.029**
	No	41 (41.8%)	33 (50%)	8 (25%)	
	Unknown	1 (1%)	0 (0%)	1 (3.1%)	
Mortality (N=98)	Alive	94 (95.9%)	63 (95.5%)	31 (96.9%)	PCS= 0.1111 *p*= 0.739
	Dead	4 (4.1%)	3 (4.6%)	1 (3.1%)	
Specific etiologies of convulsive SE^	Epilepsy	60	36	24	
	New Diagnosis of epilepsy	4	3	1	
	Prior diagnosis of epilepsy	56	33	23	
	Focal	22	13	9	
	Generalized	16	8	8	
	Mixed	14	9	5	
	Unknown	4	3	1	
	Brain malformation	7	6	1	

Category	Total population (with and without electrographic seizures)	No electrographic seizures	Electrographic seizures	Difference
	Inflammatory/autoimmune disease of the CNS	7	4	3
	Metabolic	6	3	3
	Hypoxic-ischemic encephalopathy	4	4	0
	Tumor	2	2	0
	CNS infection	1	0	1
	Sepsis	1	0	1
	Traumatic brain injury	0	0	0
	Stroke	0	0	0
	Toxin	0	0	0
	Unknown diagnosis	4	2	2
Baseline conditions^	Epileptic encephalopathy	21	12	9
	Prior neurologic disorder (not epilepsy or developmental delay/ intellectual disability)	42	30	12

^Numbers do not sum up to 98 as one patient may have had more than one condition.

Legend: CNS: Central nervous system. EEG: Electroencephalogram. **PCS**: Pearson chisquare. **SE:** Status epilepticus. **WRS:** Wilcoxon rank-sum (Mann-Whitney) test.

Table 3

Continuous electroencephalographic monitoring characteristics with a comparison of the features in patients with electrographic seizures to those without, when appropriate

Category	Total population (with and without electrographic seizures)		No electrographic seizures	Electrographic seizures	Difference
cEEG indication^	Encephalopathy with possible electrographic seizures	55	41	14	
	Management of refractory status epilepticus @	42	19	23	
	Event characterization	31	26	5	
	Management of intracranial pressure	1	1	0	
	Unknown indication	1	0	1	
EEG monitoring duration* **(N=98)**	<12 hours	13 (13.3%)	11 (16.7%)	2 (6.3%)	Pearson chisquare= 23.6043 ***p*<0.0005**
	>12–24 hours	37 (37.8%)	31 (47%)	6 (18.8%)	
	>24–48 hours	22 (22.5%)	14 (21.2%)	8 (25%)	
	>48–72 hours	5 (5.1%)	4 (6.1%)	1 (3.1%)	
	>72 hours	20 (20.4%)	5 (7.6%)	15 (46.9%)	
	Unknown	1 (1%)	1 (1.5%)	0 (0%)	
Mental status at start of cEEG (N=98)	Lethargic/obtunded/abnormal	63 (64.3%)	42 (63.6%)	21 (65.6%)	Pearson chi-square= 1.7267 *p*= 0.422
	Comatose	27 (27.6%)	17 (25.8%)	10 (31.3%)	
	Normal	8 (8.2%)	7 (10.6%)	1 (3.1%)	
Initial cEEG background (N=98)	Normal sleep	11 (11.2%)	9 (13.6%)	2 (6.3%)	Pearson chi-square= 4.5092 *p*= 0.341
	Slow disorganized	68 (69.4%)	47 (71.2%)	21 (65.6%)	
	Discontinuous	6 (6.1%)	4 (6.1%)	2 (6.3%)	
	Burst suppression	8 (8.2%)	3 (4.6%)	5 (15.6%)	
	Attenuated and featureless	5 (5.1%)	3 (4.6%)	2 (6.3%)	
Typical cEEG background (N=98)	Normal sleep	12 (12.2%)	12 (18.2%)	0 (0%)	Pearson chi-square= 15.1228 ***p*= 0.004**
	Slow disorganized	63 (64.3%)	44 (66.7%)	19 (59.4%)	
	Discontinuous	10 (10.2%)	6 (9.1%)	4 (12.5%)	
	Burst suppression	9 (9.2%)	2 (3%)	7 (21.9%)	
	Attenuated	4 (4.1%)	2 (3%)	2 (6.3%)	

Category	Total population (with and without electrographic seizures)		No electrographic seizures	Electrographic seizures	Difference
End cEEG background (N=98)	Normal sleep	18 (18.4%)	17 (25.8%)	1 (3.1%)	Pearson chi-square= 7.882 *p*= 0.096
	Slow disorganized	64 (65.3%)	39 (59.1%)	25 (78.1%)	
	Discontinuous	9 (9.2%)	5 (7.6%)	4 (12.5%)	
	Burst suppression	4 (4.1%)	3 (4.6%)	1 (3.1%)	
	Attenuated	3 (3.1%)	2 (3%)	1 (3.1%)	
Interictal epileptiform discharges (N=98)	Present	59 (60.2%)	31 (47%)	28 (88%)	Pearson chi-square= 14.7762 ***p*< 0.0005**
	Absent	39 (39.8%)	35 (53%)	4 (12.5%)	
Patterns in the cEEG^	Periodic discharges	20	7	13	
	Lateralized	7	4	3	
	Generalized	9	2	7	
	Bilaterally independent	3	1	2	
	Multifocal	0	0	0	
	Unknown	2	0	2	
	Rhythmic pattern	8	3	5	
	Lateralized	3	2	1	
	Generalized	5	1	4	
	Bilaterally independent	1	0	1	
	Multifocal	0	0	0	
	Unknown	0	0	0	
	Spike/sharp-wave	29	13	16	
	Lateralized	5	3	2	
	Generalized	10	4	6	
	Bilaterally independent	8	5	3	
	Multifocal	14	4	10	
	Unknown	0	0	0	

*EEG monitoring interruptions <12 hours are considered the same session

^Numbers do not sum up to 98 as one patient may have had more than one indication for performing a cEEG

@cEEG was performed in patients with refractory SE when it was clinically unclear that the SE had stopped (such as because of diminished or absent reactivity to stimuli).

Legend: cEEG: Continuous EEG. **SE:** Status epilepticus.

Table 4

Electrographic seizure characteristics

Frequency of electrographic seizures following convulsive SE (N=98)	Electrographic seizures	32 (32.7%)
	No electrographic seizures	66 (67.4%)
Typical duration of electrographic seizures (N=32)	10–59 seconds	11 (34.4%)
	1–5 minutes	10 (31.3%)
	6–30 minutes	7 (21.9%)
	>30 minutes	4 (12.5%)
Electrographic seizure onset localization (N=39)	Focal	16 (41%)
	Multi-focal	8 (20.5%)
	Generalized	12 (30.8%)
	Unknown	3 (7.7%)
Electrographic seizure maximal spread localization (N=34)	Focal-unilateral	13 (38.2%)
	Bilateral	17 (50%)
	Unknown	4 (11.8%)
Percent of electrographic seizures with clinical correlate (N=32)	100%	9 (28.1%)
	50–99%	2 (6.3%)
	1–49%	6 (18.8%)
	0%	11 (34.4%)
	Unknown	4 (12.5%)
Frequency of electrographic SE following convulsive SE (N=32)	Electrographic SE	15 (46.9%)
	No electrographic SE	17 (53.1%)
Type of electrographic SE (N=15)	Continuous	6 (40%)
	Intermittent	9 (60%)

Legend: SE: Status epilepticus.