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# Patients With Electrical Status Epilepticus in Sleep Share Similar Clinical Features Regardless of Their Focal or Generalized Sleep Potentiation of Epileptiform Activity

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**Abstract**

The study objective was to compare qualitatively the clinical features of patients with electrical status epilepticus in sleep with focal versus generalized sleep potentiated epileptiform activity. We enrolled patients 2 to 20 years of age, studied between 2001 and 2009, and with sleep potentiated epileptiform activity defined as an increase of epileptiform activity of 50% or more during non–rapid eye movement sleep compared with wakefulness. Eighty-five patients met the inclusion criteria, median age was 7.3 years, and 54 (63.5%) were boys. Sixty-seven (78.8%) patients had focal sleep potentiated epileptiform activity, whereas 18 (21.2%) had generalized sleep potentiated epileptiform activity. The 2 groups did not differ with respect to sex, age, presence of a structural brain abnormality, epilepsy, or other qualitative cognitive, motor, or behavioral problems. Our data suggest that there are no qualitative differences in the clinical features of patients with focal versus generalized sleep potentiated epileptiform activity.

**Keywords**

electrical status epilepticus in sleep, electroencephalogram, epileptic encephalopathy, seizures

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The frequency and distribution of interictal epileptiform activity in the electroencephalogram can be influenced by sleep. Specifically, epileptiform activity is generally potentiated during non–rapid eye movement (non-REM) sleep. This potentiation is most prominently illustrated in electrical status epilepticus in sleep, an electroencephalographic pattern characterized by a marked activation of epileptiform discharges in the transition from wakefulness to sleep. When sleep potentiation of epileptiform activity is prominent, it manifests as near-continuous slow spikes and waves that occupy a significant proportion of the non-REM sleep electroencephalogram tracing.[1-3]

The classic definition of electrical status epilepticus in sleep requires that spikes and waves occupy the electroencephalogram tracing "bilaterally" or "diffusely."[1,3] However, a persistent pattern of unilateral or focal spikes and waves during non-REM sleep has been described in several patients with electro-clinical features otherwise consistent with electrical status epilepticus in sleep.[4-6] Whether patients with unilateral or focal sleep potentiated epileptiform activity have different clinical features than patients with generalized sleep potentiated epileptiform activity has not been systematically studied.

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Our work was designed to close this gap. In a population of children with electro-clinical features consistent with electrical status epilepticus in sleep, we aimed to compare the clinical features of patients with focal versus generalized sleep potentiated epileptiform activity.

## Methods

Our study was approved by the Institutional Review Board of Children's Hospital Boston.

### Patients

We selected patients between 2 and 20 years studied between 2001 and 2009 because of a clinical suspicion of electrical status epilepticus in sleep, with at least 1 overnight electroencephalogram of a minimum duration of 18 hours at our pediatric epilepsy monitoring unit, and with sleep potentiated epileptiform activity defined as an increase of epileptiform activity of 50% or more during non-REM sleep as compared to during wakefulness.

The clinical suspicion of electrical status epilepticus in sleep was based on neuropsychological regression in at least 1 domain of development, and/or recurrent unprovoked seizures, with a typical evolution over time with seizure onset in infancy to early childhood and progressive neuropsychological regression and worsening of epilepsy during childhood.[2]

### Analysis of Clinical Data

All patients underwent neuropsychological testing at different time points of their clinical evolution. All clinical variables were extracted from the patient medical records and included demographics, clinical seizures types, and comorbid neuropsychiatric conditions. A patient was considered to have ''motor problems'' when motor deficits significantly affected his or her everyday functioning. The diagnoses of ''attention-deficit hyperactivity disorder,'' ''global developmental delay,'' ''autistic spectrum disorder,'' ''language disorder,'' and ''learning/memory problems'' were based on the results of standard neuropsychological evaluation and continued evaluation and follow-up over time by the patient's primary pediatric neurologist. ''Acquired epileptic aphasia'' was diagnosed in children with previously normal age-appropriate speech who presented with an aphasic disorder: with sub-acute onset, a progressive clinical evolution, and spontaneous fluctuations in clinical severity. A patient was considered to have ''behavioral problems'' when his or her behavior repeatedly disrupted social interactions and family life.

### Analysis of Electroencephalographic Data

All patients underwent a specific continuous electroencephalogram monitoring protocol because of the clinical suspicion of electrical status epilepticus in sleep. Patients were monitored for a period of 18 to 96 hours. Scalp electroencephalogram recordings were placed according to the 10-20 international system of electrode placement. For the purposes of our study, all electroencephalographic data were scored by 2 clinical neurophysiologists that were blinded to the clinical data. They identified the different stages of the sleep-wake cycle and randomly selected three 5-minute samples throughout wakefulness and the first 5 minutes of non-REM sleep. We have previously reported that the amount of electroencephalographic epileptiform activity during the first 5 minutes of stage II sleep correlates well with the epileptiform activity calculated overnight.[7] We used these samples to calculate spike percentage as the percentage of 1-second bins containing at least 1 spike. The electroencephalogram tracings were separately evaluated by 2 clinical neurophysiologists and, when a difference of more than 10% was found in the value of spike percentage, a review by a third clinical neurophysiologist solved the dispute. For those patients with more than 1 available night of electroencephalographic monitoring, we used the first day and night periods for calculation purposes.

For the purpose of our study, we classified the interictal epileptiform activity during non-REM sleep as focal or generalized. A patient was considered to have sleep potentiated epileptiform activity when spikes during non-REM sleep were increased by 50% or more when compared with wakefulness. All spikes were mapped on bipolar and referential montages. A hallmark feature of electrical status epilepticus in sleep is the generalization of epileptiform discharges in the transition from wakefulness to sleep so that focal discharges during wakefulness spread during non-REM sleep.[2,3] Therefore, for the purposes of this study, we classified the spikes as focal or generalized on the basis of the non-REM sleep tracing only without considering the wakefulness tracing. Patients with both focal and generalized spikes during non-REM sleep were excluded from the study. Spikes were considered focal when they had an amplitude that was $\geq$50% higher in a specific head region (involving a maximum of half of the cerebral lobes), that is, presented within 50% of falloff of the specific spike on a selected extracranial reference montage. If spikes were seen in all head regions on different montages at the same time or with less than 50% falloff, they were considered generalized (Figures 1 and 2). Patients that met the criteria for both focal and generalized sleep potentiated epileptiform activity at different points of the electroencephalogram tracing were excluded from the study.

### Analysis of Neuroimaging Data

For the purposes of our study, all magnetic resonance imaging (MRI) scans were reviewed by a pediatric neuroradiologist (SP) blinded to the clinical and electroencephalogram data.

### Statistical Analysis

We compared median age at diagnosis and median spike percentage using Mann-Whitney *U* test. Comparison of mean spike percentage values was performed with independent samples *t* test. Associations between categorical variables were assessed using chi-square or Fisher exact test as appropriate. All tests were performed at a 2-sided significance level of .05. We used SPSS 19 software (SPSS Inc, Chicago, Illinois) for all analyses.

## Results

Two hundred eight patients were studied for a clinical suspicion of electrical status epilepticus in sleep during the study period. Eighty-five patients (40.9%) met our inclusion criteria. The remaining 123 patients were excluded for further analysis because (1) their clinical evolution was not consistent with electrical status epilepticus in sleep, and/or (2) an electroencephalogram recording of at least 18 hours was not available, and/or (3) sleep potentiation of epileptiform activity did not meet the 50% cut-off threshold.

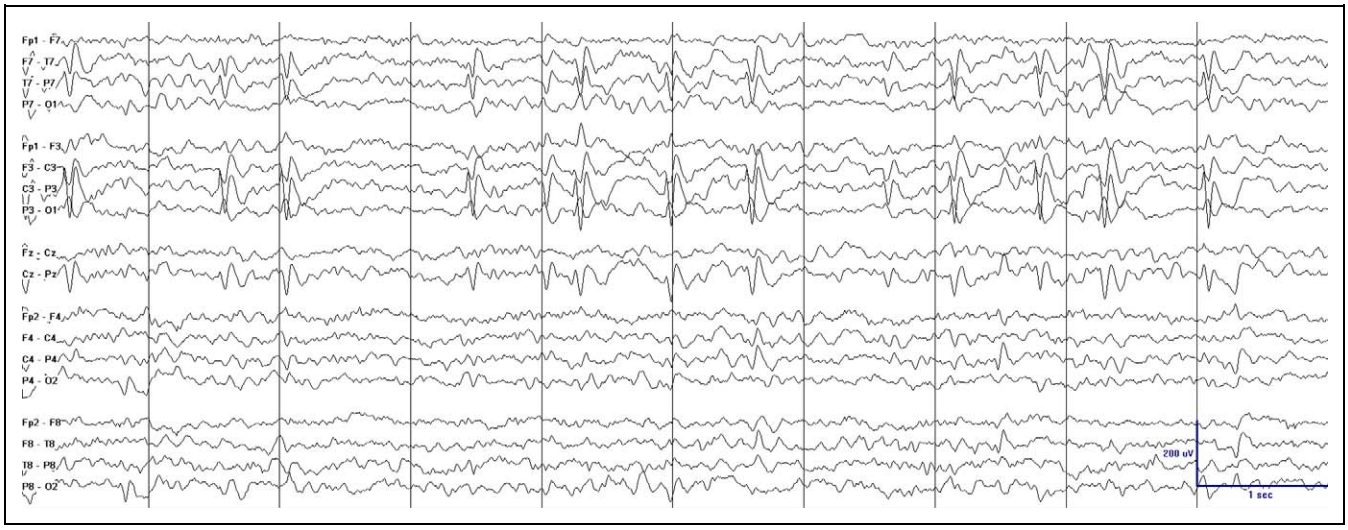


**Figure 1.** Focal sleep potentiation of epileptiform activity. During non–rapid eye movement sleep a pattern of high-amplitude continuous spikes and waves occupy the left hemisphere with a maximum in the left central and temporoparietal area. Please note the voltage scale.

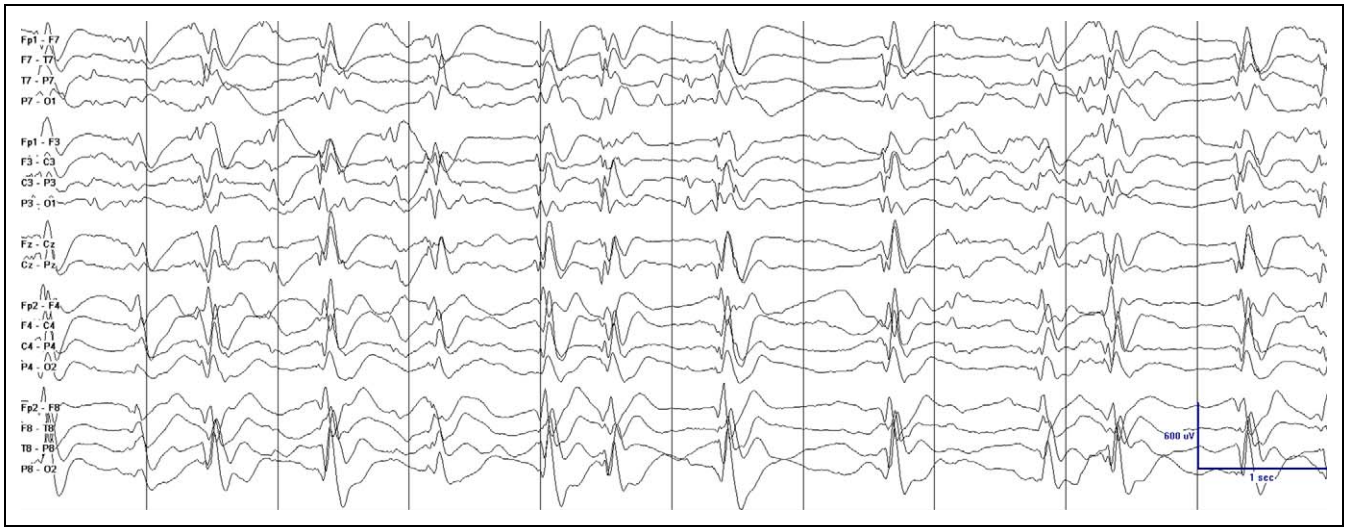


**Figure 2.** Generalized sleep potentiation of epileptiform activity. During non–rapid eye movement sleep, a pattern of high-amplitude continuous generalized spikes and waves occupy both hemispheres in an almost symmetrical distribution. Please note the voltage scale.

The median age of the patients was 7.3 years (range, 2.6-19.3 years), 54 (63.5%) were boys. Clinical features, seizure types, and associated conditions are summarized in Tables 1, 2, and 3. In addition, data on intelligence quotient scores were available for some patients (Table 4).

The sleep potentiation of epileptiform activity was focal in 67 (78.8%) patients and generalized in 18 (21.2%). There were no significant differences in demographic variables, seizure types, or clinical features between these 2 groups of patients (Tables 2 and 3). Of the 67 patients with focal sleep potentiation of epileptiform activity, the location was temporal in 24, central in 24, frontal in 16, parietal in 17, and occipital in 3 patients (the total of regions exceeds 67 as 17 patients had multifocal distribution of epileptiform activity).

In 74 of 85 patients, an MRI study was performed and, of those, a structural lesion with probable etiologic significance was found in 38 (51.4%). Fifteen of our patients had focal and lateralized lesions and 4 of them presented generalized discharges (Table 5).

**Table 1.** Clinical Features in Our Population of 85 Patients[a]

| Epilepsy | 68 (80%) |
|---|---|
| Language disorder | 39 (45.9%) |
| Global developmental delay | 24 (28.2%) |
| Autistic spectrum disorder | 18 (21.2%) |
| Motor problems | 17 (20%) |
| Acquired epileptic aphasia | 11 (12.9%) |
| Learning/memory problems | 11 (12.9%) |
| Behavioral problems | 8 (9.4%) |
| Attention-deficit hyperactivity disorder | 7 (8.2%) |

[a]Please note that the percentages do not sum up as several patients had more than 1 clinical feature.

**Table 2.** Comparison of Seizure Types in Patients With Focal and Generalized Sleep Potentiated Epileptiform Activity[a]

| Type of Seizure | Total n = 68 (100%) | Focal Sleep Potentiated epileptiform Activity n = 52 (76.5%) | Generalized Sleep Potentiated epileptiform Activity n = 16 (23.5%) | Difference |
|---|---|---|---|---|
| Absence | 30 (44.1%) | 23 (44.2%) | 7 (43.8%) | $P = .935$ |
| Generalized tonic-clonic | 25 (36.8%) | 20 (38.5%) | 5 (31.3%) | $P = 1$ |
| Complex partial | 18 (26.5%) | 14 (26.9%) | 4 (25%) | $P = 1$ |
| Tonic | 8 (11.8%) | 5 (9.6%) | 3 (18.8%) | $P = .464$ |
| Atonic | 5 (7.4%) | 3 (5.8%) | 2 (12.5%) | $P = .619$ |
| Myoclonic | 5 (7.4%) | 2 (3.9%) | 3 (18.8%) | $P = .104$ |
| Clonic | 2 (2.9%) | 2 (3.9%) | 0 (0%) | $P = 1$ |
| Aphasic | 1 (1.5%) | 1 (1.9%) | 0 (0%) | $P = 1$ |

[a]Please note that the percentages do not sum up as several patients had more than one type of feature.

**Table 3.** Comparison of the Main Demographic and Clinical Features of the Patients With Focal and Generalized Sleep Potentiated Epileptiform Activity

| Variable | Focal Sleep Potentiated epileptiform Activity n = 67 (78.8%) | Generalized Sleep Potentiated epileptiform Activity n = 18 (21.2%) | Difference |
|---|---|---|---|
| Sex, male/female | 42/25 | 12/6 | $P = .755$ |
| Median age y | 7.4 | 6.9 | $P = .809$ |
| Mean spike percentage % | 55 | 53 | $P = .786$ |
| Median spike percentage % | 50 | 55 | $P = .771$ |
| Abnormal magnetic resonance imaging | 28/58 (48.3%) | 10/16 (62.5%) | $P = .314$ |
| Epilepsy | 52 (77.6%) | 16 (88.9%) | $P = .507$ |
| Language disorder | 32 (47.8%) | 7 (38.9%) | $P = .502$ |
| Autistic spectrum disorder | 12 (17.9%) | 6 (33.3%) | $P = .195$ |
| Attention-deficit hyperactivity | 6 (9%) | 1 (5.6%) | $P = 1$ |
| Learning/memory problems | 9 (13.4%) | 2 (11.1%) | $P = 1$ |
| Global developmental delay | 18 (26.9%) | 6 (33.3%) | $P = .588$ |
| Acquired epileptic aphasia | 8 (11.9%) | 3 (16.7%) | $P = .693$ |
| Motor problems | 16 (23.9%) | 1 (5.6%) | $P = .106$ |
| Behavioral problems | 6 (9%) | 2 (11.1%) | $P = .675$ |

**Table 4.** Distribution of the Intelligence Quotients in Our Population[a]

| Type of Seizure | Focal Sleep Potentiated epileptiform Activity | Generalized Sleep Potentiated epileptiform Activity | Difference |
|---|---|---|---|
| Global intelligence quotient | 76 (n = 14) | 54 (n = 5) | $P = .015$ |
| Perceptual reasoning | 91 (n = 12) | 83 (n = 2) | $P = .189$ |
| Working memory | 83 (n = 12) | 65 (n = 2) | $P = .259$ |
| Processing speed | 83 (n = 11) | 64 (n = 2) | $P = .043$ |
| Verbal comprehension | 90 (n = 13) | 68 (n = 2) | $P = .123$ |

[a]Note that not all patients in our population had available numeric results.

## Discussion

Our data suggest that the clinical features of patients with electrical status epilepticus in sleep are qualitatively similar regardless of the focal or generalized sleep potentiation of epileptiform activity.

The age of diagnosis of the electrical status epilepticus in sleep electroencephalographic pattern in our series, 7.3 years, is consistent with previous literature indicating an average age at diagnosis of 5.4 to 8 years.[8,9] The rest of the demographic, clinical, and neuroimaging features of our population are consistent with previous literature on electrical status epilepticus in sleep.[2,8,9] Considering the patients with available data on intelligence quotient, we found a higher global intelligence quotient and higher processing speed when sleep potentiation of epileptiform activity was focal.

**Table 5.** Distribution of the Structural Brain Lesions in Our Patient Population

| Lateralized Lesions with generalized Epileptiform Activity | Lateralized Lesions With Focal Epileptiform Activity | Bilateral/Midline Lesions With Generalized Epileptiform Activity | Bilateral/Midline Lesions With Focal Epileptiform Activity |
|---|---|---|---|
| Vascular insult (hemorrhage/infarct) (n = 2) | Vascular insult (hemorrhage/infarct) (n = 6) | Rathke cyst (n = 1) | Periventricular leukomalacia (n = 15) |
| Malformation of cortical development (n = 2) | Tumor (n = 3) | Malformation of cortical development (n = 1) | Delayed myelination (n = 1) |
| | Arachnoydal cyst (n = 1) | delay/abnormal myelination (n = 2) | Holoprosencephaly (n = 1) |
| | Malformation of cortical development (n =1) | Periventricular leukomalacia (n = 2) | |

## Quantification of Epileptiform Activity

We have previously reported that the amount of electroencephalographic epileptiform activity during the first 5 minutes of stage II sleep correlates well with the epileptiform activity calculated overnight.[7] Other groups have also shown the correlation of epileptiform activity during the first 30 minutes of non-REM sleep and during the whole night counting.[4] Our method of quantification of the epileptiform activity is also supported by data demonstrating a significant correlation between the quantity of epileptiform activity during the first 5 minutes of stage II sleep and that in randomly selected samples during stage II sleep throughout the night (Table 6).

**Table 6.** Quantification of the Epileptiform Activity in Non-Rapid Eye Movement Sleep Using 2 Different Sample Periods for Calculation[a]

| Spike Frequency | Spike Frequency |
|---|---|
| First 5 minutes | Three randomly selected 100 seconds samples |
| 180 | 149 |
| 222 | 169 |
| 189 | 131 |
| 168 | 127 |
| 154 | 122 |
| 146 | 144 |
| 101 | 80 |
| 84 | 79 |
| 56 | 81 |
| 180 | 154 |
| 181 | 164 |
| 205 | 222 |
| 25 | 46 |
| 60 | 64 |
| 97 | 81 |
| 85 | 72 |
| 0 | 0 |
| 194 | 135 |
| 1 | 1 |
| 127 | 117 |
| 212 | 171 |
| 132 | 142 |
| 238 | 193 |
| 172 | 174 |
| 223 | 210 |
| 109 | 111 |
| 151 | 124 |
| 170 | 147 |

Spike frequency is the total number of spikes per 100 seconds. This table had included patients other than the ones in our manuscript and these data are only for method confirmation.

[a]We calculated the spike frequency in 2 different ways: using the first 5 minutes of non-rapid eye movement (REM) sleep and using 3 electroencephalogram samples of 100 seconds duration randomly selected throughout the non-REM sleep tracing. We compared the results in 28 tracings from 9 different patients with electrical status epilepticus in sleep. There was a high correlation in the values with Pearson correlation coefficient of 0.946, $P < .0001$.

## Quantitative Thresholds of Epileptiform Activity

Although the classical definition of electrical status epilepticus in sleep required that at least 85% of non-REM sleep should be occupied by generalized spike-wave activity,[3] different thresholds have been used.[10] For the purpose of our study, we have selected a population of patients with marked sleep potentiated epileptiform activity without requiring a specific threshold. Interestingly, their clinical and demographic characteristics did not significantly differ from previous series on electrical status epilepticus in sleep.

## Generalization of Epileptiform Activity

The classical definition of electrical status epilepticus in sleep requires the presence of generalized and symmetric epileptiform activity.[3] The International League Against Epilepsy points out that "the characteristic electroencephalographic pattern consists of continuous diffuse spike waves during slow wave sleep."[1] However, the presence of markedly asymmetric or clearly focal discharges has been described in patients with electro-clinical presentations that were otherwise consistent with electrical status epilepticus in sleep.[5,6,8,11] Veggiotti described 3 patients with unilateral continuous spike and waves and contralateral motor impairment.[6] Kramer found that of 30 patients with electrical status epilepticus in sleep, it was focal in 7 and these children were not apparently different from the rest of the patients in the series.[12] Van Hirtum-Das could not detect a different developmental pattern in children with focal versus generalized discharges.[10] However, in the literature on electrical status epilepticus in sleep, systematic comparisons between patients with focal versus generalized sleep potentiated epileptiform activity are not available. Our study qualitatively compared the

demographic and clinical features of those patients and did not find significant differences.

### *Generalized Epileptiform Activity in Patients With Focal Lesions*

Patients with electrical status epilepticus in sleep and a clearly established unilateral epileptogenic focus can present unilateral, contralateral, or generalized spikes and waves without apparent differences in surgical outcome.[13] Our results add to these findings and suggest that the clinical manifestations are similar regardless of focal or generalized sleep potentiation of epileptiform activity.[13,14]

Findings need to be interpreted in the setting of data acquisition. Data collection at a tertiary referral center may have resulted in the selection of a subpopulation of patients with more severe features, limiting the overall generalizability of our results to less severely affected patients. Retrospective data collection on demographic and clinical features may have been subject to information bias. To reduce potential bias, we reassessed the original magnetic resonance imaging and electroencephalograms when evaluating the presence of brain structural abnormalities and the calculation of epileptiform activity.

All of our patients were evaluated neuropsychologically. However, we were not able to provide a quantitative systematic comparison of the intelligence quotients for all the patients in our population. Therefore, some neuropsychological findings need to be interpreted with caution as results on standard intelligence quotients were only available for selected patients, in part because of the severe deficits in most patients. In addition, neuropsychological evaluations were often performed at other centers, and the information on neuropsychological testing was frequently summarized in a qualitative manner, making the quantitative values not available to our retrospective review.

Because of the retrospective nature of our study, we were not able to quantify the severity of the clinical features. The differences between patients with focal and generalized sleep potentiated epileptiform activity could just be a difference of severity of clinical features. However, we provide the first systematic comparison between patients with focal and generalized sleep potentiated epileptiform activity, and our findings suggest that the type of clinical features is similar in both groups. Differences in clinical severity between these groups, if any, can represent different ends of the same clinical spectrum. Further studies are needed to validate our observations and to assess whether the clinical severity is also similar.

## Conclusion

Our data suggest that in patients with electrical status epilepticus in sleep, the clinical features are qualitatively similar regardless of the focal or generalized sleep potentiation of epileptiform activity. The definition of electrical status epilepticus in sleep should consider patients with focal sleep potentiation of epileptiform activity as part of the electroclinical spectrum.

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### Author Contributions

ISF and TL designed the study. ISF, JP, MT, AR, SP, JJR, SK, and TL collected the clinical data. ISF, JP, and TL drafted the first version of the manuscript. ISF, MG, and TL participated in the statistical analysis. ISF, JP, MT, AR, SP, MG, JJR, SK, and TL revised the manuscript for important intellectual content. ISF, SP, and TL participated in the preparation of the figures.

### Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### Ethical Approval

This study was approved by the Institutional Review Board of Children's Hospital Boston.

### References

1. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia*. 1989;30:389-399.
2. Loddenkemper T, Sánchez Fernández I, Peters JM. Continuous spike and waves during sleep and electrical status epilepticus in sleep. *J Clin Neurophysiol*. 2011;28:154-164.
3. Tassinari CA, Rubboli G, Volpi L, et al. Encephalopathy with electrical status epilepticus during slow sleep or ESES syndrome including the acquired aphasia. *Clin Neurophysiol*. 2000; 111(suppl 2):S94-S102.

4. Ilic M, Akman C. Role of compressed spectral array on spike index analysis in children with electrical status epilepticus of sleep: Comparison between first 30 minutes and remaining sleep recording [Abstract]. Paper presented at 65th annual meeting of the American Epilepsy Society; 2-6 December, 2011; Baltimore, MD; A1126.
5. Saltik S, Uluduz D, Cokar O, et al. A clinical and EEG study on idiopathic partial epilepsies with evolution into ESES spectrum disorders. *Epilepsia*. 2005;46:524-533.
6. Veggiotti P, Beccaria F, Guerrini R, et al. Continuous spike-and-wave activity during slow-wave sleep: syndrome or EEG pattern? *Epilepsia*. 1999;40:1593-1601.
7. Hadjiloizou SM, Loddenkemper T, Takeoka M, et al.. A 5-minute sleep segment may be sufficient to diagnose electrographic status epilepticus of sleep (ESES) [Abstract]. Paper presented at 9th European Congress on Epileptology; June 27-July 1, 2010; Rhodes, Greece; 380.
8. Bureau M. Continuous spikes and waves during slow sleep (CSWS): definition of the syndrome. In Beaumanoir A, Bureau M, Deonna T, Mira L, Tassinari CA, eds. *Continuous spikes and waves during slow sleep. Electrical status epilepticus during slow sleep. Acquired epileptic aphasia and related conditions*. London: John Libbey; 1995:17-26.
9. Liukkonen E, Kantola-Sorsa E, Paetau R, Gaily E, Peltola M, Granström ML. Long-term outcome of 32 children with encephalopathy with status epilepticus during sleep, or ESES syndrome. *Epilepsia*. 2010;51:2023-2032.
10. Van Hirtum-Das M, Licht EA, Koh S, Wu JY, Shields WD, Sankar R. Children with ESES: variability in the syndrome. *Epilepsy Res*. 2006;70(suppl 1):S248-S258.
11. Guzzetta F, Battaglia D, Veredice C, et al. Early thalamic injury associated with epilepsy and continuous spike-wave during slow sleep. *Epilepsia*. 2005;46:889-900.
12. Kramer U, Sagi L, Goldberg-Stern H, Zelnik N, Nissenkorn A, Ben-Zeev B. Clinical spectrum and medical treatment of children with electrical status epilepticus in sleep (ESES). *Epilepsia*. 2009; 50:1517-1524.
13. Wyllie E, Lachhwani DK, Gupta A, et al. Successful surgery for epilepsy due to early brain lesions despite generalized EEG findings. *Neurology*. 2007;69:389-397.
14. Moosa A, Loddenkemper T, Wyllie E. Epilepsy surgery for congenital or early lesions. In Cataltepe O, Jallo G, eds. *Pediatric epilepsy surgery: preoperative assessment and surgical intervention*. New York: Thieme Medical Publishers; 2010: 14-23.