Optimizing Electroencephalographic Studies for Epilepsy Diagnosis in Children With New-Onset Seizures

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Objectives: To establish whether early electroencephalography (EEG) or later sleep-deprived EEG (SD-EEG) has a higher yield of epileptiform and background abnormalities in children with new-onset seizures, and to use EEG results to assist in diagnosis of electroclinical epilepsy syndromes at presentation.

Design: Prospective analysis blinded to EEG protocol and epilepsy diagnosis.

Setting: Regional service capturing a pediatric population of 121,000.

Patients: Consecutive untreated children aged 2 to 16 years presenting to emergency departments with new-onset seizures (excluding myoclonic and absence seizures).

Intervention: Each child had 2 EEG protocols: an early EEG study (within 24 hours following a seizure) and an SD-EEG study (48 hours to 4 weeks following a seizure). Epilepsy diagnosis was made independently by 2 pediatric epileptologists.

Main Outcome Measures: Rate of epileptiform abnormalities and slowing in the 2 EEG studies. The secondary outcome measure was diagnosis of epilepsy syndrome where possible.

Results: Of 92 children studied, 50 (54%) had a single seizure; 42 (46%) had 2 or more seizures at presentation. Seizures were focal in 61 children (66%) and generalized in 19 (21%). Epileptiform discharges occurred in 56 SD-EEGs (61%) and 52 early EEGs (57%) (P = .27). Background slowing occurred in 26 SD-EEGs (28%) and 42 early EEGs (46%) (P < .001). Parents preferred early EEG (65 parents [71%]) to later SD-EEG (14 parents [15%]) because of availability of earlier results and epilepsy diagnosis. Forty-two of 92 children (46%) were diagnosed with a specific electroclinical syndrome.

Conclusions: Early EEG and SD-EEG studies have a similar yield of epileptiform abnormalities. Background abnormalities are more frequent in early EEGs. The EEG results at presentation in new-onset seizures support epilepsy diagnosis, with electroclinical syndromes diagnosed in almost 50% of children.


Epilepsy Syndrome Diagnosis depends on a detailed clinical history supported by the findings on electroencephalographic (EEG) studies. Ideally, an EEG would show epileptiform activity in all children with epilepsy, but this is not the case in clinical practice. Studies of routine EEG in children with epilepsy vary in their epileptiform discharge rates from 13% to 59%.1-11 The optimal way of performing EEG studies is debated.4,12-14 It is not known whether the yield of epileptiform abnormalities is highest with early (within 48 hours) non–sleep-deprived EEG (non–SD-EEG) or late (after 48 hours) SD-EEG studies. Sleep deprivation prior to an EEG study elicits more frequent epileptiform abnormalities than a routine EEG study.1-3,6,11,15,16 It is debated whether this is due to the presence of sleep or the sleep deprivation itself.1,12,14 Of children with a normal routine EEG, 28% to 52% will have epileptiform discharges in a subsequent SD-EEG study.8,9,11,17-19 However, this increase may partially relate to test-retest variation.6,16,20

An alternative approach using early EEG was first promoted in 1998 for adults and adolescents presenting with a first seizure. King et al4 showed a significant difference, with 51% of patients having epileptiform activity on an early EEG compared with 34% of patients on routine EEG studies performed after 24 hours. Hence, we undertook a prospective study of children with new-onset seizures to
compare the yield of epileptiform abnormalities from early EEG with that from late SD-EEG. Each child underwent electroclinical assessment to make an epilepsy syndrome diagnosis.

METHODS

All children aged 2 to 16 years presenting to the emergency department with new-onset seizures were recruited. The study reflected clinical practice and recruited children who had not previously been diagnosed with epilepsy at the time their physicians requested the first EEG.

Cases were drawn from a population of 121,000 children from Wellington, New Zealand. Between January 1, 2002, and December 31, 2005, all eligible children were recruited. Pediatric and emergency physicians made an initial assessment regarding a child’s eligibility and obtained written consent. The EEG department is the sole provider of pediatric EEG services in the region and ascertains all cases of new-onset seizures. An audit of the EEG referrals was used to ascertain the number of children with new-onset seizures who were missed by the study recruitment process. The Wellington Regional Ethics Committee approved the study. Patients and their parents or legal guardians gave informed consent.

Two EEG protocols were performed on each patient: (1) an early routine EEG within 24 hours of the presenting seizure (early EEG), and (2) a later SD-EEG 48 hours to 4 weeks after a seizure. Absence and myoclonic seizures within 48 hours of the SD-EEG were allowed if the patient presented with a convulsive seizure. The EEGs were recorded using a 32-channel digital video-EEG system (E-series; Compumedics, Ltd, Victoria, Australia) with a standard 10–20 system electrode placement. Video-EEG recordings were a minimum of 30 minutes, included 4 minutes of hyperventilation, and used standard intermittent photic stimulation protocols. Children were encouraged to sleep for 10 minutes in both studies. For the SD-EEG, parents were given verbal and written instructions regarding sleep deprivation. In children older than 3 years, children were kept awake until midnight and awakened 2 hours earlier than normal. No sedation or melatonin was given. Sleep deprivation compliance was assessed by asking the caregiver how many hours the child had slept the previous night. The EEG was considered a sleep-deprived recording if the child had less than 8 hours of sleep for children aged 2 to 4 years and less than 6 hours for children aged 5 to 16 years. If the child slept more than this, another attempt at sleep deprivation was made or the child was excluded from the study.

Exclusion criteria included nonepileptic events, previous or current treatment with an antiepileptic drug, acute symptomatic seizures, or febrile seizures defined by a temperature higher than 38°C in a child younger than 6 years. Children with only absence or myoclonic seizures were excluded as it would have been difficult to obtain an EEG 48 hours after the presenting seizures given that these seizure types occur frequently and are often subtle. Children who presented with a convulsive seizure and had previously unrecognized absence or myoclonic seizures were included.

Two pediatric epileptologists (L.G.S. and I.E.S.) blinded to both the patient’s history and the EEG protocol read the EEGs independently. The presence of sleep did not discriminate between the 2 EEG studies as sleep was captured in a significant proportion of early EEGs, while some children did not sleep in the SD-EEGs. If there was a difference in interpretation, a consensus between the epileptologists was obtained. If that was not possible, a third opinion was sought.

One pediatric epileptologist (L.G.S.) assessed each child clinically following the second EEG. She completed an extensive questionnaire on the description of the event(s), possible provoking factors, medical history, and family history and examined the child. Parents and children were asked which EEG study they preferred and the reason for their preference. A magnetic resonance imaging brain scan was arranged if clinically indicated.

Two pediatric epileptologists (L.G.S. and I.E.S.) independently confirmed that the child had an epileptic seizure and was eligible for the study. Using information from the consultation, EEGs, and neuroimaging, the pediatric epileptologists independently classified the epilepsy for each child into well-recognized electroclinical syndromes and broad groups in keeping with the recent International League Against Epilepsy organization of the epilepsies.21,26 If there was a difference in diagnosis, a consensus between the epileptologists was obtained.

A 20% difference in the proportion of epileptiform abnormalities between the 2 tests was considered clinically significant in that it would alter clinical practice in terms of selection of an EEG protocol to optimize yield. This is in keeping with the study by DeRoos et al,27 who independently selected the same figure citing that approximately 20% of families report that SD-EEG was inconvenient and tiring.27 No other test was used to compare the proportion of early EEG vs later SD-EEG studies that showed either epileptiform or background abnormalities and formed the basis of the sample calculation. The sample size calculation used the percentage of epileptiform abnormalities that were different in early EEG compared with SD-EEG from exploratory data, 38% (8 of 21). A sample size of 90 would have a power of 86% if the percentage of epileptiform abnormalities found only in early EEG was 9% and those found only in SD-EEG was 29%.

RESULTS

All families of the 114 children initially identified as eligible for the study gave their consent to participate. Of the 114 children recruited, 22 were excluded due to the event being nonepileptic (10 children), antiepileptic drug treatment prior to the second EEG (6 children), inability to obtain an SD-EEG because of very frequent seizures such that a 48-hour window without seizures was impossible to obtain or because sleep deprivation itself provoked another seizure (3 children), SD-EEG being insufficiently sleep deprived (1 child), and the family withdrawing from the study (2 children).

Later audit of the EEG records identified 54 additional potentially eligible children who had not been approached for the following reasons. For 11 children, early EEG could not be performed within 24 hours due to the EEG technician’s availability. Children were missed if their family doctor arranged an outpatient assessment rather than sending them to the emergency department when they first presented. This occurred in 10 children with subtle focal seizures and in 9 children with convulsive seizures when the family was familiar with seizures. Four children received phenytoin before their first EEG, and the initial treating physician was not sure whether the event was epileptic in origin for 3 children. The reason for lack of ascertainment of the remaining 17 children is not known.

The 92 children (55 boys) who completed the study had a mean (SD) age of 8.4 (3.57) years (range, 2–14 years). Children were recruited when the diagnosis of epilepsy was first entertained. Although the practice of most pediatri-
In our region, many children were not ascertained until their second or later afebrile seizure. This occurred because the second seizure led to enrollment in the study, and previous seizures were not appreciated, or, in some cases, in pediatric practice is not to request an EEG after a first seizure.

The following electroclinical seizure types were observed: focal (61 children [66%]), generalized (19 children [21%]), and unclassified (12 children [13%]). In the 12 unclassified children, we were not able to determine whether the seizures were focal or generalized by history. The EEG results were normal in 8 of these unclassified children, and the EEGs in the other 4 children showed either nonspecific features (2 children) or both focal and generalized epileptiform abnormalities (2 children). Well-recognized electroclinical syndromes21-26 were diagnosed in 42 of 92 children (46%) (Table 1).

Early EEGs were performed 2 to 24 hours (mean, 15 hours) after the seizure, with sleep captured in 52 recordings (57%). In reality, some were serendipitously sleep deprived due to the timing of their initial seizure. The SD-EEG studies were performed a mean of 17 days following presentation. For the SD-EEG, the children slept between 4 and 8 hours (mean, 5.5 hours) before the study. Sixty-seven children (73%) slept during the SD-EEG recording, which was significantly more than the 52 children (57%) who slept during the early EEG (P = .01).

Epileptiform abnormalities were found in 52 early EEGs (57%) and 56 SD-EEGs (61%) (difference = 4%; 95% confidence interval, −3 to 14; McNemar test of observed vs expected not statistically significant, P = .27) (Table 2). Epileptiform abnormalities occurred in both EEGs in 47 children (51%) and in at least 1 EEG in 61 children (66%). When the early EEG showed epileptiform abnormalities, there was only 1 child in whom the SD-EEG gave additional information. In this child, right centrotemporal spikes were seen in the early EEG and independent right and left centrotemporal spikes were seen in the SD-EEG.

In contrast, background slowing occurred significantly more frequently in early EEGs (42 early EEGs [46%]) compared with SD-EEGs (26 SD-EEGs [28%]) (difference = 18%; 95% confidence interval, 7 to 28; McNemar test, P < .001) (Table 2). Nineteen children had slowing only on the early EEG. This was co-localized (or diffuse in the case of generalized) with epileptiform activity in 15 cases: 12 on the early EEG studies and 15 on the SD-EEG studies.

Sixty-five parents (71%) preferred the early EEG, 14 parents (15%) preferred the SD-EEG, and the remainder had no preference. Forty-six families (50%) preferred the early EEG because they anxiously sought the EEG result, and 17 families (26%) preferred the early EEG because they found sleep deprivation difficult. Some families preferred the SD-EEG because they found scheduling the EEG within 24 hours stressful and were keen to go home. Of the 61 children old enough to provide an opinion, 33 (54%) preferred the early EEG for reasons similar to those of their parents. Fifteen children (25%) preferred the SD-EEG compared with 14 parents (15%) because the children enjoyed staying up late; 13 children (21%) had no preference.

Table 1. Number of Children With Electroclinical Syndromes and Other Epilepsies

<table>
<thead>
<tr>
<th>Epilepsy</th>
<th>Broad Group</th>
<th>Syndromes</th>
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<tbody>
<tr>
<td>Electroclinical syndromes</td>
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<tr>
<td>Febrile seizures plus</td>
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</tr>
<tr>
<td>Benign epilepsy with centroparietal spikes</td>
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<td></td>
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<td>Benign occipital epilepsies</td>
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<td>Panayiotopoulos syndrome</td>
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<td>Gastaut</td>
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<td>Overlapping features</td>
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<tr>
<td>Idiopathic photosensitive occipital epilepsy</td>
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<td></td>
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<tr>
<td>Genetic generalized epilepsies</td>
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<tr>
<td>Juvenile absence epilepsy</td>
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<td>Juvenile myoclonic epilepsy</td>
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<td>Epilepsy with generalized tonic-clonic seizures alone</td>
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<td>Benign circling epilepsy</td>
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<tr>
<td>Other</td>
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<tr>
<td>Unknown epilepsies with focal seizures</td>
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<td>Unclassified seizures</td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td>92</td>
<td>42</td>
</tr>
</tbody>
</table>

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What is the optimal EEG protocol for children with new-onset seizures? There has been debate regarding the yield of routine, early, and sleep-deprived studies.2,3,12,14 With the advent of epilepsy syndrome classification, the importance of epileptiform abnormalities in confirming a specific epilepsy syndrome diagnosis has been increasingly appreciated. The aims of this study were 2-fold. First, we aimed to determine whether early EEG in children was more likely to detect abnormalities compared with late sleep-deprived recordings. Second, we used the EEG data in epilepsy diagnosis to assess the proportion of children who could be classified at presentation with new-onset seizures.

This study showed that there were no significant differences in the yield of epileptiform abnormalities between early EEG (52 children [57%]) and SD-EEG (56 children [61%]). As we did not examine routine EEG studies,
we cannot draw direct conclusions about their comparative yield. However, other studies have found variable epileptiform rates in routine EEG compared with SD-EEG and early EEG in mixed populations of children or adolescents.2,4,9,11 These studies vary as to whether the cohort studied had definite seizures, more than 1 seizure, or established epilepsy. We studied a mixed population of children with 1 or more definite seizures. Our study was designed to reflect clinical practice, focusing on when a seizure disorder was first considered in each child.

A large pediatric study showed, in a subset most closely matching our cases (aged >2 years; definite clinical seizure, although some were receiving antiepileptic drugs), that there was a higher yield for SD-EEG compared with routine EEG, although these EEG protocols were tested in different patients.2 Similarly, Leach et al4 found a higher epileptiform rate in SD-EEG than both routine EEG and sedation EEG using temazepam in the same adolescent. Another study compared the yield from early (<48 hours) SD-EEG and late SD-EEG recordings in different children but could only draw limited conclusions as only 19 of 94 children succeeded in having an early SD-EEG study.28

It is difficult to compare different studies as the cohorts in each study vary considerably. Our cohort comprises patients older than 2 years with a definite seizure, of whom 42 of 92 have a recognized electroclinical syndrome. Certain electroclinical syndromes have a higher yield of epileptiform activity on EEG studies than others and are activated by specific provocateurs; these factors would strongly influence the yield of epileptiform abnormalities. One strength of our study was that it used each child acting as his or her own control rather than using 2 separate cohorts that each had 1 protocol.2 A further differentiating point was that all subjects had both protocols regardless of whether results of the first study were normal.5,8,11,15 To our knowledge, this is the first study to directly compare early EEG with later SD-EEG in the same patient. The yield of epileptiform abnormalities did not differ between protocols; however, the early EEGs were significantly more likely to have background abnormalities. Nineteen children had slowing only on their early EEG, which is likely to reflect postictal change. Although postictal focal slowing may be diagnostically helpful in adults,13 this was not the case in our study.

Many EEG studies focus on the importance of epileptiform abnormalities in determining whether a patient is at risk for further seizures. While this emphasis is drawn from adult studies, the key issue in pediatric studies is to consider the diagnosis of specific epilepsy syndromes that carry an EEG signature. For example, the finding of centrotemporal spikes in a child with a rolandic or convulsive seizure supports a syndrome diagnosis of benign epilepsy with centrotemporal spikes; this is crucial in informing management and prognosis. We found that almost 50% of children could be diagnosed with a specific electroclinical syndrome.

Advantages and disadvantages of performing each study protocol were identified. Overall, families preferred the early EEG because of the earlier availability of results. In general, partial sleep deprivation is well tolerated and safe, although some families report irritability in their children and inconvenience associated with ensuring that their child is sleep deprived.3,17,28,29 To assess the degree of negative feelings that families experienced about sleep deprivation, we asked a hypothetical question about whether they would prefer a blood test or an SD-EEG if similar information could be obtained from each test. All children and parents preferred sleep deprivation. Indeed, many parents commented that their children are often sleep deprived in daily life because of illness and social reasons.

From a practical point of view, children with new-onset seizures are often admitted to hospital or spend significant time in the emergency department, and timing an early EEG is not difficult. In some centers, however, scheduling an EEG within 24 hours of a seizure may not be practical owing to EEG technician availability. For these departments, a scheduled SD-EEG within the next 4 weeks may permit better use of their resources. Our findings suggest that both approaches provide similar results, so choice should be guided by service and economic preference.

International guidelines and recommendations for EEGs after new-onset seizures vary markedly.13,14,30-35 Some advocate early EEG studies within 48 hours of a seizure, others suggest initial routine EEG followed by SD-EEG if normal, and still others recommend an SD-EEG or sleep study. There is also debate as to whether an EEG should be recommended after the first or the second seizure. Our study was not designed to consider this issue. Our findings suggest that in children with new-onset seizures, there is no difference between the epileptiform discharge rate found in EEGs performed within 24 hours of a seizure and later SD-EEGs. Our epileptiform rates are greater than those found in routine EEGs in published studies,2,4,5,8-10 and as other studies have found higher rates in SD-EEGs or early EEGs than in routine EEGs,2,4,5,8-10 we can infer that both early EEG and SD-EEG protocols are preferable to routine EEGs in new-onset seizures. In practice, both protocols are well tolerated and easy to perform. Improving the yield of epileptiform abnormalities enhances the clinician’s ability to make an early epilepsy syndrome diagnosis in children presenting with new-onset seizures. This in turn optimizes management and prognostic counseling.

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REFERENCES