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Value of combined video EEG and polysomnography in clinical management of children with epilepsy and daytime or nocturnal spells

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ABSTRACT

Purpose: Sleep disorders are common in epilepsy. Additionally, events of staring, jerking, or nocturnal behaviors are common presentations in neurology or sleep practice. Moreover, sleepiness and nocturnal awakenings are common symptoms in children with epilepsy and differentiation form ongoing seizures and sleep disorders is needed. However, limited data exist for the best evaluation methods. This study evaluated the usefulness of combined video electroencephalography (EEG) and polysomnography (PSG) studies (vEEG/PSG).

Methods: Polysomnography custom database was searched for combined vEEG/PSG studies, performed from July 2010 to April 2014, which identified 240 studies. From chart review, data were collected for presenting symptoms, sleep disorder and epilepsy/neurology diagnoses, and EEG and PSG results.

Results: Most common indications for performing combined vEEG/PSG were correlating sleep events with seizure occurrence, evaluating sleepiness, nocturnal awakenings and nocturnal events. Sleep physician evaluation and/or PSG were abnormal in 94% of the studies. The EEG was abnormal in 53% and events or seizures were recorded in 40% of the studies. Hence, vEEG/PSG addressed the diagnostic questions. Additionally, as compared to children with epilepsy, a significantly larger number of children with spells/parasomnia had a normal sleep evaluation including a normal PSG (9 Vs 37%, $p = 0.00003$).

Conclusions: This study demonstrates that combined video EEG and polysomnography is useful in addressing the common management questions in children with epilepsy and suspicious nocturnal events. Additionally, sleep disorders are more common in children with epilepsy than parasomnia. Hence sleep evaluation is important in children with epilepsy. Further prospective studies are needed.

1. Introduction

Sleep disorders are common in children with epilepsy, with some reports suggesting that the prevalence of sleep disturbances is as high as 45% within this group [1,2]. However, limited data exists regarding the screening, evaluation, and management of potential sleep disorders in children with epilepsy. Additionally, patients presenting with nocturnal events are common in both epilepsy and sleep medicine clinics. These presentations may represent parasomnias or seizures and differentiating between the two can be difficult without a comprehensive evaluation. Moreover, other common presenting symptoms of sleep disorders can sometimes to be difficult to differentiate from unwitnessed seizures such as daytime sleepiness and nocturnal awakenings. Furthermore, correlation of onset of sleep event and seizure onset is sometimes needed for appropriate management of either of the disorders such as sleep apnea and hypoxia precipitating seizures, or nocturnal epileptiform discharges causing jerks in sleep. The standard montage used in diagnostic polysomnography (PSG), which includes bilateral frontal, central, and occipital leads referenced to the mastoid processes [3], is limited in its ability to accurately identifying seizure or nocturnal events when compared to extended EEG montages [4]. Recently, a study described the utility of using an extended EEG montage during polysomnography in an adult sleep lab [5]. However, similar data has not been reported for children.

Abbreviations: EEG, electroencephalogram; OI, obstructive Index; RDI, respiratory disturbance index; CSA, central sleep apnea; EKG, electrocardiogram; CO2, carbon dioxide; AASM, American Academy of Sleep Medicine; MSLT, multiple sleep latency test; REM, rapid eye movement sleep; ICSD, international classification of sleep disorders; OSA, obstructive sleep apnea; NREM, non- REM; PLMD, periodic limb movement disorder; RLS, restless leg syndrome; BECTS, benign epilepsy with centro-temporal spikes

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We performed this study to identify the usefulness of performing combined video EEG and polysomnography (vEEG-PSG) in children with epilepsy and to compare our data with the existing adult literature.

2. Methods

The retrospective study was approved by the local institutional review board. The custom built polysomnography database was searched for combined vEEG/PSG studies, performed from July 2010 to April 2014. The inclusion criteria included patients aged 1 month to 18 years, both male and female gender, all ethnicities and the studies performed during the specified time period. The exclusion criteria included subjects who did not have a clinical evaluation with a sleep physician performed or missing data. If a subject had multiple combined vEEG-PSG studies performed, only initial study was included in the study. Database search also provided date of birth, gender, reported polysomnography results, and diagnoses (including neurologic disorders and types of epilepsy). Chart review was conducted to identify presenting complaint for sleep evaluation, confirm the sleep and epilepsy diagnoses, reasons for performing EEG and reported EEG results. Most of the studies were clinically reviewed by one physician (SVJ) with standard reporting template.

The combined Video EEG and polysomnography (vEEG-PSG) were performed simultaneously in the epilepsy monitoring unit using Stellate software system (Natus Medical Inc.; Pleasanton, CA). Video EEGs utilized the international 10–20 placement of electrodes with 18 channels to collect overnight video EEGs. For polysomnography, subjects were studied for up to 12 h in a quiet dark room with an ambient temperature of 24 °C, in the company of their parents. Subjects went to bed at their routine bedtime. The following parameters were recorded simultaneously: body position, bilateral electro-occulogram, electroencephalogram, chin and anterior tibialis electromyogram, tracheal microphone, electrocardiogram, pulse oximetry (Masimo; Irvine CA), thoracic and abdominal inductance plethysmography, nasal pressure transducer and end-tidal carbon dioxide (CO_2). Sleep stages were scored by a certified sleep technologist according to the American Academy of Sleep Medicine (AASM) guidelines [3]. The multiple sleep latency test (MSLT) was performed the following day after the nighttime PSG in a dark quite room with an ambient temperature of 24 °C. The test consisted of a 5- nap opportunity separated by 2-hour intervals. The following parameters were recorded simultaneously: body position, bilateral electro-occulogram, electroencephalogram, electrocardiogram, chin and anterior tibialis electromyogram. Sleep stages were scored by a certified sleep technologist according to the American Academy of Sleep Medicine (AASM) guidelines [3].

The following definitions were used for the diagnosis of sleep disorders based on international classification of sleep disorders (ICSD-2) [6].

1) Central sleep apnea (CSA) was diagnosed if apnea hypopnea index (AHI) was 5 or more and predominant events were central in origin. Apnea hypopnea index was defined as the number of apneas and hypopneas per hour of the total sleep time.
2) Hypoventilation was diagnosed if the end tidal CO_2 level was > 50 mm Hg for more than 25% of the night.
3) Hypersomnia was diagnosed if excessive daytime sleepiness was associated with mean sleep latency of 8 min or less on multiple sleep latency test (MSLT).
4) Insomnia was diagnosed if the PSG did not suggest any other sleep disorder and the subject had clinical signs and symptoms of insomnia consistent with international classification of sleep disorders (ICSD) criteria. Hence, the children with insomnia had abnormal clinical evaluation and sleep study showed disturbed sleep but without any specific sleep disorders.
5) Nocturnal hypoxemia was diagnosed if more than 30% of the study showed oxygen saturation of less than 90%.
6) Narcolepsy with cataplexy was diagnosed if excessive daytime sleepiness was associated with cataplexy and multiple sleep latency testing showed a mean sleep latency of 8 min or less and sleep onset REM periods in 2 or more naps.
7) Obstructive sleep apnea (OSA) was diagnosed if the obstructive index (OI) was 1 or more. OI was defined as the number of obstructive apneas and hypopneas per hour of the total sleep time.
8) Parasomnia: non-REM (NREM) arousal parasomnia were included in this category and included night terrors, sleep walking, and confusional arousals.
9) Periodic limb movement disorder (PLMD) was diagnosed if the periodic limb movement index was more than 5 per hour during the polysomnography and if there was a clinical history of sleep disturbance or daytime sleepiness.
10) Primary snoring was diagnosed if subjects with a history of snoring had no polysomnographic evidence of obstructive sleep apnea or hypoventilation.
11) Restless leg syndrome (RLS) was diagnosed as defined by international classification of sleep disorders (ICSD-2) criteria for definite RLS in children and adolescents [6].

2.1. Statistical analyses

Descriptive statistics were used to evaluate the presenting complaint and final diagnosis associated with each PSG. Fisher's exact test was used for comparison of distribution of sleep disorders between the parasomnia and epilepsy cohorts (SAS, Cary NC).

3. Results

A total of 240 combined vEEG/PSG studies were identified being performed on 240 subjects. Among 240 subjects, 139 subjects had epilepsy, 42 subjects had daytime or nocturnal events/spells, 46 had neurological disorders, which included, autism, Arnold-Chiari malformation, brain tumor, headache/migraine and muscular dystrophy, and 13 had other disorders, which, included apneic episodes and pulmonary disorders. Characteristics of the subjects and results are represented in Table 1.

The patients were referred for sleep evaluation by neurologist, epileptologists, pulmonologists and primary care physicians. The polysomnogrphy studies were ordered per clinical guidelines for the diagnosis of sleep disorders. The presenting symptoms for sleep evaluation are listed in Table 2. The most common symptoms prompting sleep evaluation and most common symptoms prompting the EEG evaluation, polysomnography results and EEG results for individual sleep complaints are presented in the Table 3a (for cohort with epilepsy) and Table 3b (for cohort without epilepsy).

The following were the most common indications for combined vEEG/PSG.

1) To correlate the sleep events with occurrence of seizures: We identified that sleep disorders precipitated seizures in only a few cases in our cohort. In several patients, due to frequent sleep events and seizures, it was not possible to determine if one lead to other. In rare cases, the seizures were associated with central apneic events. In

Table 1
Characteristic of the group and analysis.

Characteristic	N (%)
Total studies	240 (100)
Age- mean (SD)	9.8 (5.8)
Gender m: f	140 (58) : 100 (42)
Epilepsy type	G: 35 (25%), F: 60 (43%), U: 44 (32%)

G: generalized, F: focal, U: undetermined as to focal or generalized.

Table 2
Distribution of the presenting symptoms for sleep evaluation.

Presenting symptom	N (%)
Sleep related breathing problems	72 (30)
Difficulty falling asleep and/or nighttime awakenings	52 (21.6)
Events/Spells	36 (15)
Movements in sleep	26 (10.8)
Sleepiness	21 (8.8)
Follow up OSA/PAP	13 (5.4)
Nocturnal seizures	5 (2.1)
Other	15 (6.2)

OSA: Obstructive sleep apnea; PAP: positive airway pressure titration.

Table 3a
Synopsis of the most common results for the epilepsy cohort, based on the most common presenting symptoms for sleep evaluation.

	Sleep related breathing disorder	Nocturnal awakenings	Sleepiness
Sleep disorder diagnosis			
OSA (n)	21	6	2
Insomnia (n)	9	15	4
PS (n)	16	5	1
EEG reason			
Seizure characterization (n)	10	3	7
Correlate sleep with seizures (n)	8	5	0
New spells (n)	13	6	5
Nocturnal events (n)	10	4	1
EEG results			
Epileptiform spikes (n)	23	16	11
Seizures (n)	21	6	1
Normal (n)	13	10	6
Non-epileptic events with abnormal EEG (n)	1	3	0

OSA: obstructive sleep apnea; PS: primary snoring.

Table 3b
Synopsis of the most common results for the non-epilepsy cohort, based on the most common presenting symptoms for sleep evaluation.

	Sleep related breathing dis	Awakenings and or difficulty falling asleep	Spells
Sleep disorder diagnosis			
OSA (n)	9	2	7
Insomnia (n)	1	17	2
PS (n)	4	1	1
Parasomnia	2	2	10
EEG reason			
Single seizures (n)	2	2	1
Spells suspicious of seizure (n)	11	7	19
Neurological dis (n)	9	8	4
EEG results			
Epileptiform spikes (n)	3	6	6
Seizures (n)	1	0	0
Normal (n)	1	22	6
Non-epileptic events with abnormal EEG (n)	1	3	3

OSA: obstructive sleep apnea; PS: primary snoring.

rare cases, bursts of epileptiform abnormalities led to limb movements on polysomnography. In patients with vagus nerve stimulator, respiratory events were associated with stimulation on-time.

2) Nocturnal spells which were difficult to differentiate as seizures or parasomnia from clinical history: In most cases without epilepsy, even in patients with abnormal EEGs, the events were identified as parasominas. In patients with epilepsy, the nocturnal events were more likely to be seizures.
3) Nocturnal awakenings, which were difficult to differentiate from sleep disorder Vs ongoing unwitnessed seizures by clinical history: In most cases, nocturnal awakenings were related to sleep disorders such as obstructive sleep apnea or insomnia as well as parasomnia.
4) Daytime sleepiness, which was difficult to differentiate sleep disorder Vs ongoing unwitnessed seizures by clinical history: To our surprise, many children presenting with sleepiness and epilepsy had PLMD. Interictal EEG spike wave activity was also noted in patients with sleepiness. We rarely identified seizure in children with sleepiness and epilepsy.
5) Nocturnal apnea which was of unclear etiology: Both seizures and CSA were common in these children.
6) Convenience- patients requiring prolonged EEG to characterize ongoing seizures, to evaluate response to medication, to ascertain readiness of weaning of medication or to identify if spells are seizures and symptoms suggestive of sleep disorders.

A few parents had requested that both testing be performed simultaneously to avoid school absences for multiple days.

3.1. Sleep Evaluation/results

Table 2 shows the presenting complaints for sleep evaluation. A sleep evaluation consisted of a clinical evaluation by a sleep physician and a polysomnography. The most common presenting symptoms for sleep evaluation were for suspected sleep-disordered breathing (30%) followed by difficulty falling asleep and/or nighttime awakenings in 21.6% of the patients. (Table 2). Presenting complaints listed as “Other” included oxygen desaturation on home nocturnal pulse oximetry study and respiratory diseases such as asthma, pneumonia etc. Polysomnography was abnormal in 94% of the 240 studies. Table 4 shows the sleep disorder diagnosis for the cohort. The most common diagnoses were obstructive sleep apnea and/ or hypoventilation. Multiple sleep latency testing (MSLT) was performed on 4 subjects, 3 of which were diagnosed with hypersomnia and one was diagnosed with narcolepsy with cataplexy.

3.2. Distribution of sleep disorders

Table 4 shows the distribution of sleep disorder diagnosis in the entire cohort. Multiple sleep disorders were seen in 45 subjects in the cohort. Table 5 compares the sleep disorders in children with epilepsy and children with spells/events or parasomnia. As compared to children with epilepsy, a significantly larger number of children with spells/parasomnia had a normal sleep evaluation including a normal PSG (9 Vs 37% Vs 9%, $p = 0.00003$) When patients with insomnia were excluded, there was still a significant difference between normal studies in children with events/spells when compared to subjects with epilepsy (41% Vs 12%, $p = 0.0001$).

Table 4
distribution of sleep disorder in the cohort.

Sleep disorder	N (%)
Total study number	240 (100)
CSA + Nocturnal Hypoxemia	19 (6.5)
Hypersomnia + Narcolepsy with cataplexy	4 (1.4)
Insomnia	55 (19)
Inadequate study	5 (1.7)
Normal	14 (4.8)
OSA+ Hypoventilation	82 (28.3)
Parasomnia	35 (12.1)
PLMD + RLS	31 + 1 (10.8)
PS	37 (12.8)
Other	3 (1)

CSA: central sleep apnea; OSA: obstructive sleep apnea; PLMD: periodic limb movement disorder; RLS: restless leg syndrome, PS: primary snoring.

Table 5
Comparison of sleep evaluation between children with epilepsy and spells/parasomnia [children with other neurological disorders excluded].

	Epilepsy n (%) [total n = 139]	Spells/ Parasomnia (n %) [total n = 49]	p-value
Sleep disordered breathing	70 (50)	19 (38)	0.143
Insomnia	32 (23)	5 (10)	0.063
PLMD + RLS	18 (13)	4 (8)	0.603
Hypersomnia + Narcolepsy with cataplexy	3 (2)	1 (2)	1.0
Normal PSG	13 (9)	18 (37)	**0.00003**
Normal PSG (Excluding patients with insomnia from both groups)	13 (12)	18 (41)	**0.0001**
Other	3 (2)	2 (4)	0.64

* Fisher Exact test.

Table 6
Yield of testing in respect to abnormality.

Characteristic	N (%)
Abnormal PSG/clinical evaluation	226 (94)
Abnormal PSG [excluding subjects and studies with insomnia]	169 (91.4)
Abnormal EEG	127 (52.9)
Events or seizures recorded on EEG	96 (40)
Seizures recorded on EEG	41 (17)
Diagnosis of non-epileptic event: parasomnia: seizures	50(20.8) : 5 (2) : 41 (17.0)

Electroencephalogram (EEG).

3.3. Epilepsy/EEG results

EEG abnormalities were seen in 53% of the combined vEEG/PSGs (Table 6). Of the abnormal EEGs, seizures were seen in 32%, epileptiform discharges in 56% and focal slowing in 12%. The remaining 45% of EEGs were normal, of which 26.5% captured events of concern. Either an event or seizure was recorded in 40% of the studies. These included seizure recording in 17%, parasomnia recording in 2% and non-epileptic events in 20.8% of the studies. The non-epileptic events were events of staring, dizziness etc. which were not seizures, based on EEG.

3.4. Yield of testing

Table 6 shows the yield of testing in this cohort. The sleep evaluation/polysomnography was abnormal in 94%, EEG was abnormal in 53% and seizures/events were recorded in 40% of the studies. Ninety-one percentages of studies were abnormal when studies with insomnia were excluded.

4. Discussion

We performed this study to report the use of combined video EEG and polysomnography in children. While there are other studies evaluating the use of vEEG/PSG in children with nocturnal frontal lobe epilepsy and attention deficit hyperactivity disorder (ADHD), our study focused on a clinical cohort of children with suspicious night time events, epilepsy or other neurological disorders [7–9]. Most common reasons to perform the combined vEEG/PSG were to correlate sleep events with onset of seizures, to evaluate nocturnal events including awakenings and apnea, and to evaluate daytime sleepiness. Our study showed that the combined vEEG/PSG were useful in answering these questions. Our study also demonstrated that combination of clinical sleep evaluation and combined vEEG/PSG was valuable in diagnosing sleep disorder in 94% of studies, EEG abnormalities in 53% of the studies and capturing an event or seizure in 40% of the studies. Hence, the combined vEEG/PSG were able to address the diagnostic question in most patients.

4.1. Indications for combined video EEG and polysomnography

In clinical management of epilepsy, patients frequently present with overlap of symptoms of sleep disorders. Symptoms such as daytime sleepiness may be caused by ongoing seizures or a sleep disorder. Nocturnal awakening may represent a sleep disorder but may also be caused by an unwitnessed seizures. Nocturnal movements may be related to epileptic myoclonic jerks or PLMD. While sleep events such as apnea leading of hypoxia may precipitate seizures, apnea may also be associated with seizures. It will be important to differentiate these for appropriate management. Moreover, sleep disorders are common in children with epilepsy. Sleep evaluation may require a polysomnography [10,11]. Additionally, children with epilepsy may require prolonged video EEG during the course of their disease to confirm diagnosis, evaluate additional events/spells, quantify seizure frequency, evaluate the drug response, and assess the readiness for medication wean [12,13]. Moreover, nocturnal and daytime events/spells are common presentation in neurology and/or sleep practice. In these cases, a differentiation between sleep disorder, seizure or non-epileptic event is needed [14]. Performing both video EEG and polysomnography together addresses the differentiation of sleep disorders from seizures or other events. Moreover, it is convenient and saves time for the families.

4.2. The value of combined video EEG and polysomnography

A standard video EEG includes 18 channels, which are digitally recorded to allow events to be reviewed using a variety of montages. The review is performed at 30 mm/sec paper speed. A standard polysomnography montage utilizes 6-channel EEG and includes bilateral frontal, central, and occipital electrodes referenced to contralateral mastoid processes. It is typically reviewed at 10 mm/sec paper speed. The temporal, parietal, and midline head regions are underrepresented in these studies. In a study in adults, ictal and other event recordings were compared in 18- channel standard EEG Vs 8-channel montage. Of note, the 8 channel montage included temporal EEG electrodes which are not typically included in polysomnography montages. The results showed that 18-channel EEG was significantly better for seizure detection, seizure localization and for differentiation of seizures and non-epileptic events. Additionally, localization of seizures based on lobe of origin was improved with 18-channel EEG especially for temporal and parieto-occipital seizures [4]. Furthermore, it is commonly noted that the alpha and beta frequency ictal patterns are likely to be incorrectly classified as arousals in the typical polysomnography. Additionally, benign epilepsy with centro-temporal spikes (BECTS) is one of the most commonly occurring epilepsy in children. It is likely to miss these spikes in the absence of temporal electrodes as maximal spike amplitudes may be seen in central or temporal electrodes [15]. In the absence of midline and temporal electrodes, it may be difficult to differentiate central spikes from vertex waves. Hence, it is important to use these electrodes in children with suspected or proven epilepsy. In our study, 75% children had focal epilepsy or undetermined epilepsy and 40% studies had events/spells or seizures recorded. We presume that we would have missed identification and diagnosis if only a standard polysomnography

was performed.

A recent study in adults reviewed data from extended EEG and polysomnography. In 237 subjects, 93% of the subjects had a sleep disorder diagnosis and 38% had abnormal EEG. Obstructive sleep apnea was the most common sleep disorder and it was significantly more common in subjects with epilepsy compared to subjects without prior history of seizures [5]. Our study showed similar results with 94% of the clinical sleep evaluation and PSG results suggestive of sleep disorder, 53% of abnormal EEG and 40% of the EEG studies with events/ spells or seizures captured. Hence, the usefulness of combined polysomnography and EEG in children is similar to the reported data in adults.

4.3. Distribution of sleep disorders in epilepsy

In our study the distribution of sleep disorders between the entire cohort and the epilepsy subgroup were similar to the reported data in the literature. The most common presenting symptoms and diagnoses were related to sleep related breathing disorders. In a study, 33% of the patients with refractory epilepsy had obstructive sleep apnea [16]. In another study in children with epilepsy, obstructive sleep apnea was found in 42% of patients referred for sleep related complaints [17,18]. Additionally, we identified restless legs syndrome or periodic limb movement disorder in 11% and insomnia in 19% of children with epilepsy. In studies periodic limb movements/ disorder has been reported in 15% of adults [19] and 10% of the children with epilepsy [17]. In adult patients with epilepsy, restless leg syndrome was identified in 18–35% [19,20]. No data exist for restless leg syndrome in children with epilepsy. In a questionnaire based study, onset and maintenance insomnia was reported in 34 and 52% of the subjects with epilepsy respectively [20]. Hence, the data supports that sleep disorders are common in epilepsy. Moreover, studies suggest that treatment of sleep disorders may improve seizure frequency in this population [21,22]. Hence a sleep evaluation is important in patients with epilepsy.

Sleep disorders are common in epilepsy as discussed above. Also, sleep disorders are common in children with parasomnia. In a study, 61% of children with parasomnia were found to have another sleep disorder such as sleep disordered breathing (SDB) and less frequently restless legs syndrome- periodic limb movement disorder (RLS-PLMD) [23]. In our study, 94% of the children with epilepsy had abnormal clinical sleep evaluation and PSG as compared to 63% in the spells/ parasomnia group. This difference was highly significant. This again underscores the importance of screening for sleep disorders in children with epilepsy. Additionally, parasomnia is also common in patients with epilepsy. In our study, 10 subjects had both disorder. In patients with nocturnal frontal lobe epilepsy, 30% had arousal parasomnia and 12% of subjects had REM behavioral disorder [24]. Hence, differentiating parasomnia and nocturnal seizures is not only very important but also challenging.

The limitations of our study include retrospective nature and inclusion of patients who were referred for sleep evaluation.

5. Conclusions

The study showed that combined video EEG and polysomnography are useful in answering commonly presented management challenges of differentiating sleep symptoms from ongoing seizures, correlating abnormalities between sleep disorder and seizures, differentiating non-epileptic events, parasomnias from seizures and identifying coexisting sleep disorders in patients with epilepsy. Further studies may focus in identifying protocols for performing these studies.

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