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# Validation of actigraphy with continuous videoelectroencephalography in children with epilepsy



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# ABSTRACT

*Background:* The relationship between epilepsy and sleep is bidirectional as seizures disrupt sleep and coexisting sleep disorders have detrimental effects on seizure control and quality of life for both the children and their families. Previous research has reported on sleep disturbance in children with epilepsy primarily by subjective parental reports. Actigraphy may provide a more accurate objective evaluation of sleep, but the validity of this sleep measure for children with epilepsy has not yet been assessed. The primary objective of this study was to validate the use of actigraphy as a tool in studying sleep patterns in children with epilepsy.

*Methods:* This was a prospective study comparing sleep and wake epochs recorded for 24 h simultaneously by actigraphy and by continuous video-electroencephalography (VEEG) monitoring in 27 patients aged 2–18 years with medically refractory epilepsy.

*Results:* Strong correlations were found between actigraphy and VEEG sleep variables including night sleep period (r = 0.99), night sleep time (r = 0.96), duration of night wake time (r = 0.93) and number of significant wakings during the night (r = 0.81).

*Conclusion:* The study results validate that actigraphy is a reliable and objective clinical and research tool for evaluating sleep and wakefulness in children with epilepsy.

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# 1. Introduction

Sleep disorders are among the key factors influencing the quality of life (QOL) of children with medically refractory epilepsy and their families [1,2]. Clinicians who manage children with refractory epilepsies must focus not only on seizure management but also on other significant factors influencing the QOL of both the child and his/ her family, one of which is evaluation and treatment of sleep disturbance. Current research has established bidirectional correlations between epilepsy and sleep [3,4]. Sleep–wake cycles and the different stages of sleep are associated with varying frequency of clinical seizure occurrence [5–11]. Sleep influences not only seizure frequency but is also associated with an increase in the occurrence of abnormal brain electrical discharges (interictal epileptiform discharges) [12]. Sleep deprivation is known to be strongly

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correlated with an increased frequency of interictal epileptiform discharges and seizures in both healthy subjects and in patients with epilepsy [13,14]. Alternatively, epilepsy can have a profound effect on the sleep–wake cycle, sleep architecture, and presence of sleep disorders including an increased incidence of parasomnias, nighttime awakenings, longer sleep latency, daytime sleepiness, and altered sleep habits such as co-sleeping and parental presence at sleep onset in children with epilepsy [15].

Although sleep disorders have a significant influence on patients with refractory epilepsy, there is a major gap in well-designed studies in this field. Investigating sleep patterns in children with epilepsy is limited to studies using subjective parental reports and sleep diaries. Only limited studies have been done using objective outcome measures for sleep with overnight polysomnography (PSG) [16].

Overnight PSG is considered the most reliable objective tool for studying sleep. This multi-parametric test collects data from several physiologic monitors including electroencephalography (EEG), electromyography (EMG), electro-oculography (EOG), and cardiorespiratory channels, which are then analyzed visually to define wake epochs, sleep stages, and causes of sleep disruption [17]. However, this method is labour intensive and expensive due to its specialized equipment which contributes to long wait-times for the study [18]. Furthermore, it can be challenging to collect reliable data using PSG with children who have neurological disabilities (e.g. autism spectrum disorder, cognitive delay, or epilepsy), since they are more likely to be resistant to instrumentation, and sensitive to changes in their sleep location [19]. Children with refractory epilepsy will commonly undergo continuous video EEG (cVEEG) monitoring in an in-patient setting. This method enables electrographic characteristics of the seizure disorder and evaluation, localization, and quantification of interictal epileptic discharges. VEEG also evaluates many of the physiologic monitors used by the PSG including video monitoring, EEG channels, and EMG, thus enabling detailed assessment of sleep characteristics.

Over the last two decades, actigraphy has become an important objective technique to measure sleep/wake states both in sleep research and in clinical sleep medicine. Actigraphy involves the use of a portable watch-like device worn on the wrist that records movement over extended periods of time, which is used to infer time spent asleep and wake. The benefits of using actigraphy in sleep research are many: it is easy to use, the cost is low, and it can be worn at home for extended periods of time. According to practice parameters published by the American Academy of Sleep Medicine in 2007 [20], actigraphy provides an acceptably accurate estimate of some sleep measurements in normal healthy adults. However, the validity of actigraphy in special populations is more challenging and thus warrants further investigation. Although this practice parameter was published in 2007, the conclusion concerning the need to validate actigraphy in populations such as children with epilepsy remains [21,22]. The studies of sleep in children with epilepsy have documented the significant effects of epilepsy on sleep architecture. It is not known how interictal epileptiform discharges, subclinical seizure activity, or even the motor activity associated with a clinical seizure will be recorded by an actigraph. Therefore comparing actigraphy to VEEG which captures these changes in electrographic and motor signals is an ideal method of validating the use of actigraphy in this population.

The aim of this study was to validate actigraphy as an objective measure to study sleep–wake patterns in children with epilepsy by comparing actigraphy measurements with measurements collected by continuous VEEG monitoring.

# 2. Methods

#### 2.1. Subjects and setting

This was a prospective cohort study in the inpatient epilepsy monitoring unit (EMU) of a tertiary care pediatric hospital (The Hospital for Sick Children, Toronto). Children aged 2-18 years who were expected to be in the EMU for  $\geq$ 24 h and had refractory epilepsy were eligible for inclusion. Medically refractory epilepsy was defined by one or more seizures within 6 months prior to enrollment as patient despite adequate trials of two or more anti-epileptic medications in the past. All families of children who met these criteria were contacted by the research assistant by telephone 1 week prior to their elective admission in the EMU, and on the day of admission they were approached to consider participation. The study was approved by the Hospital Research Ethics Board. Children with epilepsy plus motor or movement disorders such as quadriplegic cerebral palsy, dystonia, chorea, or tremor (which may have affected the validity of the actigraphy data) or those who could not cooperate with wearing an actigraph were not eligible for inclusion in the study.

After obtaining consent, the subject's parent or caregiver completed screening questionnaires. These included a questionnaire designed for this study to obtain demographic data as well as information on the subject's epilepsy, medical and surgical history, and symptoms of sleep disorders.

# 2.2. Actigraphy validation

Subjects wore the actigraph continuously on the non-dominant wrist while simultaneously being evaluated with cVEEG. During the cVEEG recording, the subjects have a 2 m electric cord which connects the EEG leads to the outlet and therefore must stay in bed or close to the bed in the hospital room. This ensures that sleep/ wake status as well as seizures are both recorded electrographically and are simultaneously videotaped. The information from the cVEEG was recorded continuously, and reviewed and analyzed for ictal and interictal data by the neurologist and neurophysiologist. Sleep stages were scored visually on a computer screen using standard criteria [23]. Both the cVEEG and the actigraphy were scored by 1 min epochs for sleep/wake state independently. The scoring was done in a blinded method for both the actigraphy and the cVEEG by two reviewers independently. Measurements collected by cVEEG monitoring served as the gold standard for comparison.

### 2.3. Actigraphy

The actigraphy used in this study was the Motion Sleep Watch (Ambulatory Monitoring Inc., Ardsley, NY, USA). Data were downloaded to the computer and analyzed using Action 4 software. Actigraphy data were analyzed by activity counts to determine sleep versus wake time using Sadeh sleep scoring PCD ZCM [24,25].

### 2.4. cVEEG and analysis of sleep parameters

Scalp EEG recording was performed using the 10-20 international system of electrode placement. Subjects were videotaped, and EMG and EOG channels were recorded, allowing accurate sleep evaluation. cVEEG data analysis software (Harmonie, Version 7; Stellate Systems Inc., Montreal, Canada) enables an easy platform for analyzing and annotating brain wave background activity, ictal and interictal epileptiform discharges, and for analyzing each significant event during the EEG recording. The interictal epileptiform discharges (IED) were quantified. There is no one accepted method for quantifying amount of IED [26,27]. In this study, IED index was measured by calculating the number of seconds with IEDs per 100 s. For each patient, we have measured IEDs in 20 randomly sampled epochs of 20 s during wakefulness and stage I-II NREM sleep and then averaging the samples for a final IED index. IEDs are known to be more frequent in localization-related epilepsy (as in our subjects) in NREM stages N1 and N2. Therefore these are the stages of sleep which were evaluated in this study [28].

Although the core VEEG data recorded contain relevant information regarding the sleep stages, the Harmonie, Stellate Systems Inc. (Version 7) which was used for EEG analysis is not suitable for performing efficient epoch-by-epoch sleep analysis as is routinely done with PSG software. Thus, the EEG data were downloaded to Compumedics Profusion PSG software. This software enables accurate analysis of sleep stages in each epoch. Sleep stages are scored visually on a computer screen using standard criteria [23,29]. An Excel data file was created with wake/sleep stage of each epoch. Both sets of data, from PSG and from the actigraphy, were then downloaded to the Action 4 software (Ambulatory Monitoring Inc.) for further correlational analysis.

#### 2.5. Correlations between common sleep variables

Validation analysis of the actigraphy was conducted by comparing commonly measured sleep and daytime activity actigraphy parameters elaborated in Table 1 [30–32] with the corresponding

#### Table 1

Comparison of actigraphy and video-EEG monitoring.

Variable	Actigraph	Video-EEG monitoring
Sleep onset	First of at least three consecutive minutes of sleep during bedtime scored by actigraph algorithm	First bedtime epoch scored as sleep using standard EEG criteria
Sleep offset	The time of the last five consecutive minutes of sleep before awakening	First epoch post night sleep scored as awake using standard EEG criteria
Sleep period	The elapsed interval (in hours) from sleep onset to sleep offset defined by actigraph	The elapsed interval (in hours) from sleep onset to sleep offset defined by EEG
Total sleep time	The total number of 1 min epochs scored as sleep by the actigraph	The total number of 1 min epochs scored as sleep based on standard EEG criteria
Number of wakings after sleep onset	Number of one or more consecutive epochs post night sleep onset scored as awake by actigraph algorithms	Number of one or more consecutive epochs post night sleep onset scored as awake using standard EEG criteria
Number of significant wakings after sleep onset	Number of epochs of ≥5 min post night sleep onset scored as awake followed by ≥15 min scored as sleep by actigraph algorithms	Number of epochs of ≥5 min post night sleep onset scored as awake followed by ≥15 min scored as sleep using standard EEG criteria
Percent time asleep during the day	Percent of epochs scored as asleep of all available epochs for scoring between 09:00 and 19:00 by actigraph algorithms	Percent of epochs scored as asleep of all available epochs for scoring between 09:00 and 19:00 by EEG algorithm

EEG, electroencephalography.

parameters measured by the cVEEG using Pearson correlations. The usual sleep parameters described in the literature were evaluated in this cohort: sleep onset, sleep offset, sleep period, total sleep time, number of wakings after sleep onset, number of significant wakings after sleep onset, and percent time asleep during the day. This allowed identification of which sleep and daytime activity parameters were accurate and valid. These variables were chosen based on current recommendation for more uniform measurements in actigraphy studies to enable comparability between studies [33].

#### 2.6. Statistical analysis

Bland–Altman plots (difference plot) were composed for the parameters measured. *t*-Tests were performed to evaluate significant bias. Pearson's correlations were used to evaluate associations between sleep variables measured by actigraphy and by VEEG.

# 3. Results

# 3.1. Subject characteristics

The subjects' demographic information (including developmental level as reported by parents), and parental report of symptoms of sleep disorders, are summarized in Table 2. In this cohort, the average participant age was 9.3 years (range, 3-17 years). Parental reports indicated that sleep problems were present in 12 of 27 children (44%). The most frequently occurring sleep disturbance reported was waking from sleep with nocturnal seizure. This was primarily in children aged >9 years (eight of the nine subjects), whereas difficulties in falling asleep was the second most frequent difficulty, being mainly reported in children aged <9 years (three of the four children). All children (as in the inclusion criteria) in this cohort had medically refractory epilepsy with frequent seizures. Six of 27 (22%) reported daily seizures, and 11 of 27 (41%) reported weekly seizures. Sixteen of the 27 subjects (59%) reported more than one seizure type, with an average of 2.1 seizure types per patient. Eighteen of the subjects were taking two or more anti-seizure medications. The majority of subjects included in this cohort had a reported delay in at least one of five domains (gross motor, fine motor, speech and language cognitive development, or activities of daily living).

# 3.2. Video-EEG monitoring

This study included a total of 1904 h of recordings with an average of 70.5 h per subject (Table 3). During this time, 103 seizures were captured in the 27 subjects and 87% of the subjects demon-

strated interictal epileptiform discharges. An IED index, measured by analyzing the number of interictal epileptiform discharges on multiple randomized epochs during wakefulness and stage 1–2 sleep, demonstrated that IEDs were commonly recorded. There were sig-

#### Table 2

Patients' characteristics.

Demographics	
No. of subjects	27
Age (years) (mean ± SD)	$9.3 \pm 4.2$
Sex	19 M, 8 F
Racial background	
White	22
East Asia	1
More than 1	2
Other	2
Weight (kg) (mean ± SD)	$42.5 \pm 35.3$
No. of siblings (mean ± SD)	1.5 ± 1.2
Reported sleep disorders	
Overall	12
Sleep onset	4
Waking at nights	3
Early morning wakening	2
Woken by seizures	9
Seizure history	
Age at onset (months) (mean ± SD)	$35.9 \pm 30.2$
No. of different seizure types (mean $\pm$ SD)	2.1 ± 1.2
Reported seizure types (no. of patients)	
Generalized tonic clonic	10
Atonic	4
Absence	11
Myoclonic	2
Simple partial	9
Complex partial	8
Secondary generalized	3
No. of current AED (mean ± SD)	$2\pm1$
No. of past AED (mean ± SD)	$2.5 \pm 2.1$
Reported developmental delay	
Patients with delay/no delay	19/8

SD, standard deviation; AED, anti-epileptic drugs.

#### Table 3

Video-electroencephalography analysis.

Total hours recorded	1904
Hours recorded per patients (mean ± SD)	$70.5\pm22.4$
Total no. push buttons	168
Total no. SZ captured	103
No. of patients with IED during study	22
IED <sup>a</sup> index during day	3.9
IED <sup>a</sup> index during stage 1–2 sleep	10.4

SD, standard deviation; SZ, seizures; IED, interictal epileptiform discharges.

 $^{\rm a}\,$  Average number of seconds with interictal epileptiform discharges per 100 s.

nificantly more IEDs during stage 1–2 NREM sleep as compared to wake. During wake there was an average of 3.9 s with IEDs per 100 s vs 2.7 times more during stage 1–2 NREM sleep.

# 3.3. Correlations between common sleep variables

Commonly measured sleep and daytime activity actigraphy and VEEG parameters are compared in Table 1. Very strong correlations were found for night sleep period (r = 0.99), night sleep time (r = 0.96), duration of night wake time (r = 0.93), and percent time of sleep during the day (r = 0.99) (Fig. 1). Bland–Altman plots of these parameters are shown in Fig. 2. There were no significant differences (t-test) between actigraphy and vEEG measurements of night



**Fig. 1.** Strong linear correlations found between actigraphy and videoelectroencephalography for different variables examined including night sleep period, night sleep time, duration of night wake time and percent time of sleep during the day. PSG, polysomnography.



**Fig. 2.** Bland–Altman plots of different variables examined including night sleep period (bias 3.5, SD 15.77 from –27 to 34), night sleep time (bias 8.3, SD 31 from –53 to 69), duration of night wake time (bias –4.8, SD 31.1 from –49 to 40) and percent time of sleep during the day (bias 0.3, SD 1.3, from –2.1 to 2.9). There were no significant differences between all presented measurements.

sleep period, night sleep time, duration of night wake time, and percent time of sleep during the day.

Moderate correlation (Fig. 3) was found for number of wakings after sleep onset (WASO, r = 0.53); however, strong correlation was



**Fig. 3.** Moderate correlation was found between actigraphy and videoelectroencephalography for number of wakings after sleep onset (WASO); however, strong correlation was found for number of significant wakings after sleep onset (SWASO).

found for number of significant wakings after sleep onset when only more significant wakings were counted (SWASO, r = 0.81).

#### 3.4. Seizures and actigraphy correlations

One hundred and three seizures were captured during the study period in 13 of the 27 participants. Seizure duration ranged between 1 and 142 s with an average of 24 s and SD of 36 s. More than 90% of the seizures captured had a motor component. To examine whether the number of seizures captured during the study influenced the performance of the actigraphy, a correlation analysis was conducted separately for children with captured seizures. Figures 4 and 5 demonstrate the correlation analysis and Bland–Altman plots for key parameters in children with captured seizures. In this cohort (children with seizures) there were strong correlations found on actigraphy data for night sleep period (r = 0.99), night sleep time (r = 0.97), duration of night wake time (r = 0.93), and percent time of sleep during the day (r = 0.99). Despite children having seizures during the evaluation, strong correlations were found for number

# 4. Discussion

This study demonstrates that actigraphy is a valid and reliable method of evaluation for studying sleep–wake cycles in children with epilepsy, including those children who have frequent IEDs and both sleep and wake seizures. Actigraphy is based on assessing motor ac-



**Fig. 4.** Analysis done separately for children with captured seizures. Very strong linear correlations found between actigraphy and video-electroencephalography for different variables examined including night sleep period, night sleep time, duration of night wake time, and percent time of sleep during the day.



**Fig. 5.** Analysis done separately for children with captured seizures. Bland– Altman plots of different variables examined including night sleep period (bias –0.2, SD 9.6 from –19 to 19), night sleep time (bias 4.9, SD 27 from –49 to 58), duration of night wake time (bias –5.1, SD 22.9 from –50 to 40) and percent time of sleep during the day (bias 0.2, SD 1.7, from –3 to 3.6). There were no significant differences between all presented measurements.

tivity patterns. Epileptic activity can generate unique movement patterns that may have impact on activity-based scoring. Therefore, it is important to assess the validity of actigraphic scoring in this unique population. Sleep parameters examined by actigraphy correlated with the same parameters evaluated by VEEG. This was true in children with frequent IEDs, and in children with frequent seizures, as was demonstrated by a separate analysis done for 13 subjects with a total of 103 seizures captured at the time of the study. Although the majority of the seizures analyzed had a motor component, as reported by others [34] seizures in this cohort also tended to be short in duration (average length, 25 s). Thus they did not have significant influence on the actigraphy performance.

Children with medically refractory epilepsy often have developmental delay and more significant etiologies for their epilepsy than children with epilepsy who are not medically refractory. Previous work has established the reliability and validity of actigraphy in sleep/ wake detection, particularly in typically developing infants, children, and adults [35–37]. However, recent publications have raised concerns about the validity of sleep-wake scoring algorithms in specific populations such as infants [38], children with intellectual deficits and motor handicaps [39] or in patients with tetraplegia [40]. Parents of 19 subjects in this study reported delay or had documented delay in the medical chart in at least one of the following fields: gross motor, fine motor, cognitive, speech, or activities of daily living. The subjects in our study, in addition to having developmental disabilities, also had more complicated epilepsy, including more seizures, and more abnormal interictal patterns. By reporting on the validity of actigraphy in this cohort, we predict that this would also be a valid method of sleep/wake analysis in children with less severe forms of epilepsy.

This is the first prospective study validating the use of actigraphy in children with epilepsy. This is valuable, as actigraphy is a reliable tool to measure sleep objectively, and sleep (and sleep deprivation) has significant implications for children with epilepsy. Correlations between sleep variables including night sleep period and time, and duration of wake during sleep, were very strong. A strong correlation was also found for number of SWASO when only significant wakings after sleep onset (≥5 min) were included, but not for WASO when any epoch scored as wake was included. Therefore, we conclude that actigraphy is reliable for estimating all sleep parameters examined except WASO.

Published actigraphic validation studies using PSG as the gold standard only include "time in bed" whereas the main advantage of actigraphy is in documenting sleep–wake patterns continuously over 24 h periods across both day and night. Our study is unique as we validated actigraphy for 24 h with VEEG, allowing the opportunity to capture long epochs of wake (as well as sleep) data. In addition, subjects were not restricted to bed rest during the waking recordings, but could move about in the epilepsy monitoring room during waking. There was a very strong correlation between actigraphy and VEEG in the percent time asleep during the day.

Epilepsy represents one of the most frequently occurring neurologic problems in children. The relationship between sleep and epilepsy has been extensively studied [4,41,42], but further research in this area is needed, particularly in the area of intervention. This study supports using actigraphy for further research that will allow the evaluation of children with epilepsy and sleep disorders, and monitor the efficacy of clinical intervention trials.

### 5. Conclusion

Studying sleep in children with epilepsy using objective methods is important due to the significant bidirectional relationship between epilepsy and sleep. Actigraphy is an excellent method to study sleep and wake in children, including those with comorbid developmental difficulties, as it is relatively inexpensive, readily available, and accurate. In addition, using actigraphy in this population in future research will allow further exploration of the relationship between epilepsy and sleep. This study demonstrated that actigraphy is a valid tool for studying sleep–wake patterns in children with epilepsy. Actigraphy is an excellent method to evaluate sleep parameters including total sleep time, total sleep period, duration of WASO, and the number of SWASO. Actigraphy is not reliable for evaluating number of WASO for children with refractory epilepsy. Actigraphy reliably estimates wake and sleep not only during the night but also during the day. The actigraphy analysis was accurate in this cohort of children with medically refractory epilepsy, including those who had brief seizures during the recordings.

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#### **Conflict of interest**

Avi Sadeh has served as a consultant for Johnson & Johnson. The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.04.021.

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