Automated Assessment of Sleep in Patients With Dravet Syndrome From Simulated Behind-the-Ear EEG

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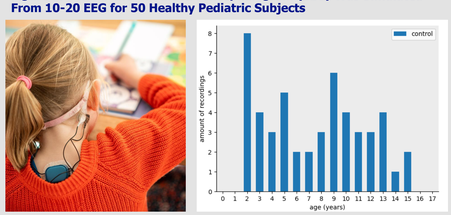
Introduction

- Poor sleep is an under-evaluated but highly relevant comorbidity in children with epilepsy[1,2]
- A typical montage to assess sleep in a clinical setting uses an elaborate setup of electroencephalogram (EEG), electromyogram (EMG), and electrooculogram (EOG) electrodes
- This is not only intrusive, especially for children, but also limits examinations to single-night sessions
- To facilitate long-term monitoring, also including daytime naps, a less intrusive setup would be required, such as a behind-the-ear electrode setup as this is well tolerated by the patients and can be discreetly used during the day[3]

Objective

- This study explores the feasibility of automated pediatric sleep staging from simulated behind-the-ear EEG in healthy subjects and patients with Dravet syndrome (**Figure 1**)

Figure 1. Behind-the-Ear Electroencephalogram (EEG) Was Simulated From 10-20 EEG for 50 Healthy Pediatric Subjects



Left panel: Example of a behind-the-ear EEG setup in a pediatric subject.
Right panel: The histogram of the pediatric subjects included in the study.

Methods

- 50 overnight EEG recordings from pediatric subjects (without epileptic abnormalities during the recorded period) were selected from a dataset from Saint-Luc University Hospital (Brussels, Belgium)
- Three independent experts manually scored sleep staging (Wake, N1, N2, N3, REM [Rapid Eye Movement])
- Behind-the-ear montage was simulated from 9 additional recordings that had simultaneous 10-20 scalp and behind-the-ear EEG (provided by Byteflies)
- Different sleep staging models were trained for automated sleep scoring (Wake, N1, N2, N3, REM), including: EEG subset of 8 electrodes (M1), electrocardiogram (ECG [M2]), EEG subset + ECG (M3), the simulated behind-the-ear EEG (M4), and simulated behind-the-ear EEG + ECG (M5; **Figure 2**)
  - This algorithm included the extraction of several features and a gradient-boosting model for classification
- Performance evaluation in the healthy cohort was based on Cohen's kappa coefficient (κ) using a 5-fold cross-validation strategy
- The inter-expert agreement was used as baseline performance
- The sleep staging performance on overnight EEGs from 20 pediatric patients with DS, collected at the Antwerp University Hospital (Belgium), was evaluated by comparing it to the sleep scoring of a single expert

Overview

QUESTION

What is the reliability of a behind-the-ear electrode electroencephalogram (EEG) for evaluating sleep staging in pediatric patients with Dravet syndrome (DS)?

INVESTIGATION

- A typical montage to assess sleep in a clinical setting uses an elaborate setup
- This study explores the feasibility of automated pediatric sleep staging from simulated behind-the-ear EEG in healthy subjects and patients with DS

Behind-the-ear EEG was simulated from 9 recordings that had both 10-20 EEG and behind-the-ear EEG from healthy pediatric subjects

Fifty 24-hour epilepsy-free EEG recordings from healthy pediatric subjects were selected from a dataset from Saint-Luc University Hospital (Brussels, Belgium)

Sleep staging models were trained for automated sleep scoring (Wake, N1, N2, N3, REM) for the 8-electrode EEG and the simulated behind-the-ear EEG

The sleep staging performance on overnight EEGs from 20 patients with DS, collected at the University Hospital Antwerp (Belgium), was evaluated by comparing it to the sleep scoring of a single expert

EEG, electroencephalogram; REM, Rapid Eye Movement sleep state.

- We trained different sleep staging models (including 8-electrode EEG and behind-the-ear EEG) using expert consensus scoring
- Model performance was assessed by Cohen's kappa (k) between the model's classifications and the consensus scoring of 3 experts
- 5-fold cross-validation was used for performance on the control cohort; performance of the DS cohort was extracted directly
- Differences (and *P* values) between the modalities were assessed using (2-sided) Wilcoxon rank-sum test, and differences across the modalities using (2-sided) Wilcoxon signed-rank test

RESULTS

- A typical montage to assess sleep in a clinical setting uses an elaborate setup
- This study explores the feasibility of automated pediatric sleep staging from simulated behind-the-ear EEG in healthy subjects and patients with DS

Table. Agreement of EEG Sleep Staging Models Compared to Consensus Scoring in the Healthy Population and the Scoring of One Expert in Patients With DS

	Control (n=50)	DS Cohort (n=20)	Difference
8-electrodes EEG model	κ=0.82±0.09	κ=0.77±0.21	*P*=0.022
Behind-the-ear EEG model	κ=0.76±0.10	κ=0.69±0.18	*P*=0.038
Difference	*P*<0.001	*P*=0.277	N/A

DS, Dravet syndrome; EEG, electroencephalogram; N/A, not applicable.

- In the healthy pediatric population (n=50), sleep staging (5-stages) was accurate with simulated behind-the-ear EEG
  - N3 sleep was the easiest sleep stage to detect because of the widespread slow-wave activity
- In the 20 patients with DS, good performance of sleep staging was achieved using simulated behind-the-ear EEG

CONCLUSIONS

- This study demonstrates that sleep can be reliably assessed from a behind-the-ear EEG montage in an automated way in both healthy subjects and patients with DS

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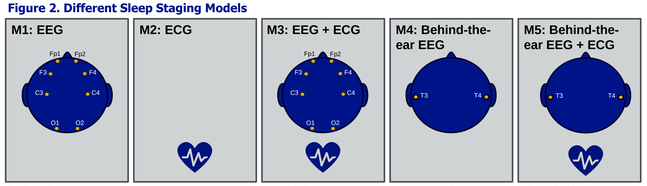
Figure 2. Different Sleep Staging Models

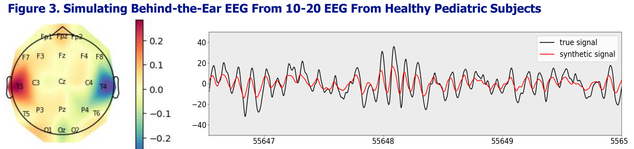


The five different sleep staging models that have been built. Model 1 (M1) uses 8 EEG electrodes; model 2 (M2) uses 1 bipolar ECG lead; model 3 (M3) uses 8 EEG electrodes and 1 bipolar ECG lead; model 4 (M4) uses a bipolar behind-the-ear derivation; and model 5 (M5) uses behind-the-ear EEG and ECG.
ECG, electrocardiogram; EEG, electroencephalogram.

Results

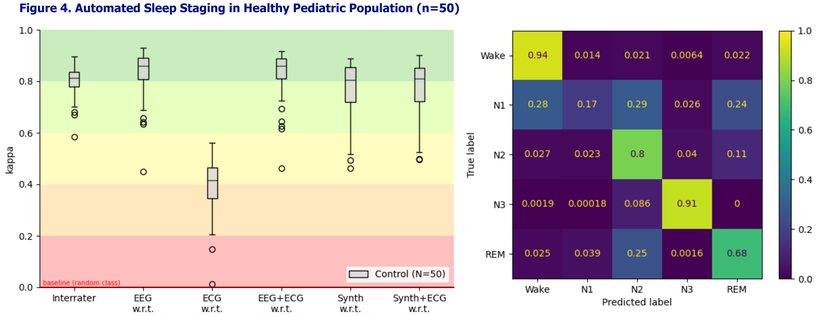
- The average ordinary least-squares (OLS) solution suggested using a bipolar derivation of channels T3 and T4 to estimate the behind-the-ear EEG from the 10-20 EEG (**Figure 3**)
- The amplitude of the bipolar signal is furthermore reduced by 70% to match the reference behind-the-ear signal

Figure 3. Simulating Behind-the-Ear EEG From 10-20 EEG From Healthy Pediatric Subjects



Left panel: Average OLS solution to simulate a behind-the-ear montage from 10-20 scalp EEG. Colors indicate the weights that were assigned to each channel.
Right panel: Overlay of true and synthetic behind-the-ear signals show matching waveforms and periodicity.
EEG, electroencephalogram; OLS, ordinary least-squares.

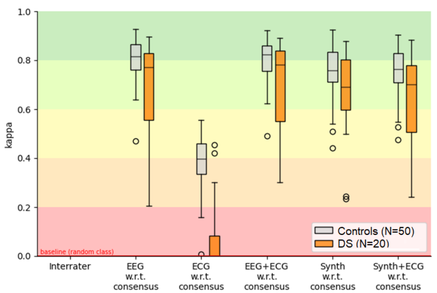
Figure 4. Automated Sleep Staging in Healthy Pediatric Population (n=50)



The performance of the five different sleep staging models in healthy subjects. The left panel shows the performance compared to interrater consensus using Cohen's kappa. The right panels shows the confusion matrix for sleep staging with behind-the-ear EEG.
ECG, electrocardiogram; EEG, electroencephalogram.

- **Sleep staging (5-stages) can be accurately obtained with simulated behind-the-ear EEG (Figure 4)**
- REM staging is more difficult with behind-the-ear EEG; not surprising, since EOG and chin EMG patterns are the major discriminators for REM
- N2 slightly underestimated; this is likely because spindles and k-complexes have a frontocentral distribution
- N3 is the easiest sleep stage to detect, because of the widespread slow-wave activity

Figure 5. Automated Sleep Staging in Pediatric Patients With DS (n=20)



The performance of the five different sleep staging models in pediatric patients with DS. The performance of the automated sleep staging is compared to the scoring of one expert rater using Cohen's kappa.
DS, Dravet syndrome; ECG, electrocardiogram; EEG, electroencephalogram.

- **Good performance of sleep staging is achieved in patients with DS with the simulated behind-the-ear EEG (Figure 5)**
  - For all models, the performance drops slightly when translating to patients with DS, and the variability increases.
  - The drop in performance is mainly because the N2 and REM agreements are reduced

Conclusions

- This study demonstrates that sleep can be reliably assessed from a behind-the-ear EEG montage in an automated way in both healthy pediatric subjects and patients with DS
- Compared to the 8-electrode EEG solution, the behind-the-ear montage results in a slightly decreased performance especially for REM staging, but the obtained hypnograms maintain substantial agreement with expert scoring
- The slight decrease in performance and increase in variability in the DS cohort might be explained by the fact that the neural signals are more contaminated due to epileptic abnormalities
- Nevertheless, this study has shown the potential to algorithmically quantify sleep staging in DS, which is foundational for long-term sleep monitoring using non-intrusive wearable hardware

References

1. Stores, G., Wiggs, L., Campling, G. (1998). Sleep disorders and their relationship to psychological disturbance in children with epilepsy. Child: care, health and development, 24(1), 5-19.
2. Manni, R., & Terzaghi, M. (2010). Comorbidity between epilepsy and sleep disorders. Epilepsy research, 90(3), 171-177.
3. Libenson, M. H., Haldar, A., & Pinto, A. L. (2014). The stability of spike counts in children with interictal epileptiform activity. Seizure, 23(6), 454-456.

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Disclosures

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