INTRAVENOUS DEXAMETHASONE IMPROVES SLEEP PHYSIOLOGY IN CHILDREN WITH GENETIC DRUG-RESISTANT EPILEPSY

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INTRODUCTION

Corticosteroids and adrenocorticotrophic hormones (ACTH) are the therapy of choice to treat infantile spasms (1).

However, systematic studies about their use in other types of childhood epilepsies remain rare and ACTH can have serious side effects (2,3).

This study compares the epileptic burden in children with genetic drug-resistant epilepsy (DRE) before and after a standardized treatment with pulsatile corticoid therapy (PCT) using an objective and subjective approach.

METHODS

- Standardized protocol for PCT with cycles of high-dose dexamethasone (20mg/m^2 body surface) intravenously during 3-day hospitalization per cycle
- 24 children with genetic drug-resistant epilepsy (10 female; 6.2 $\pm$ 3.4 y)
- Sleep scoring of EEG recordings obtained during hospitalization according to AASM criteria (4)
- Automatic detection of sleep spindles (10–16 Hz, 0.5-3s) with a validated spindle detector (5)
- Minimum duration criterion of 1 minute of N2 sleep in baseline EEG and EEG at the end of PCT → n=14 patients with spindle detections
- Categorization of fast spindles (12–16 Hz) and slow spindles (10–12 Hz)
- Epileptic burden (% of EEG with spikes) was compared before and after PCT
- Subjective evaluation in a standardized interview

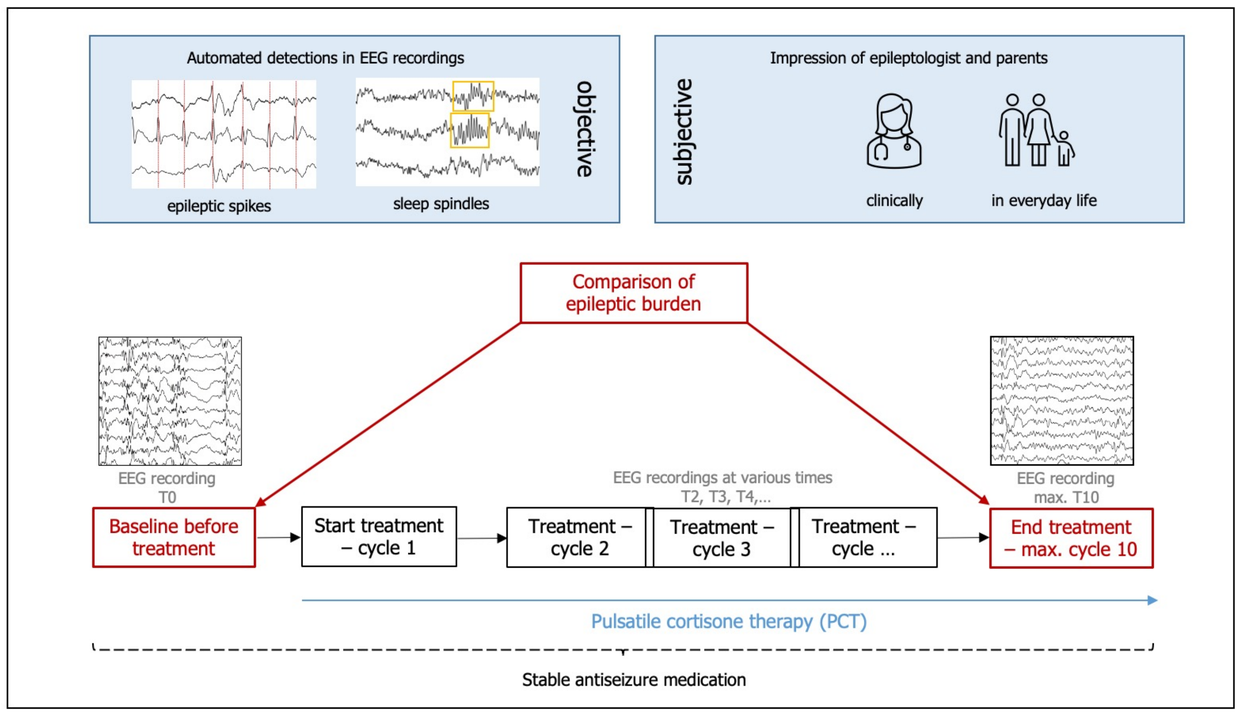

Figure 1. Study design.

RESULTS

- Slight increase of all spindle rates in the EEG after PCT compared to the baseline EEG (1.0/min [0-3.2] vs. 1.6/min [0.2-3.9], p=0.054, d=0.27)
- Significant increase of fast spindle rates after PCT (0.8/min [0-2.2] vs. 1.5/min [0.2-3.4], p=0.015, d=0.36)
- No difference in slow spindle rates after PCT (0.3/min [0-1.2] vs. 0.3/min [0.1-0.5], p=0.407, d=0.04)
- Improvement of seizure frequency in 17 patients (85.0%), no improvement in 3 patients (15.0%), n.a. in 4 patients
- One patient became seizure free
- Greatest improvements from the parents' perspective in quality of life (19 of 24 children, 79.2%), cognition (17 of 22 children, 77.3%), attention/alertness (13 of 18 children, 72.2%) and sleep (13 of 16 children, 81.3%)
- No serious adverse effects, well tolerated

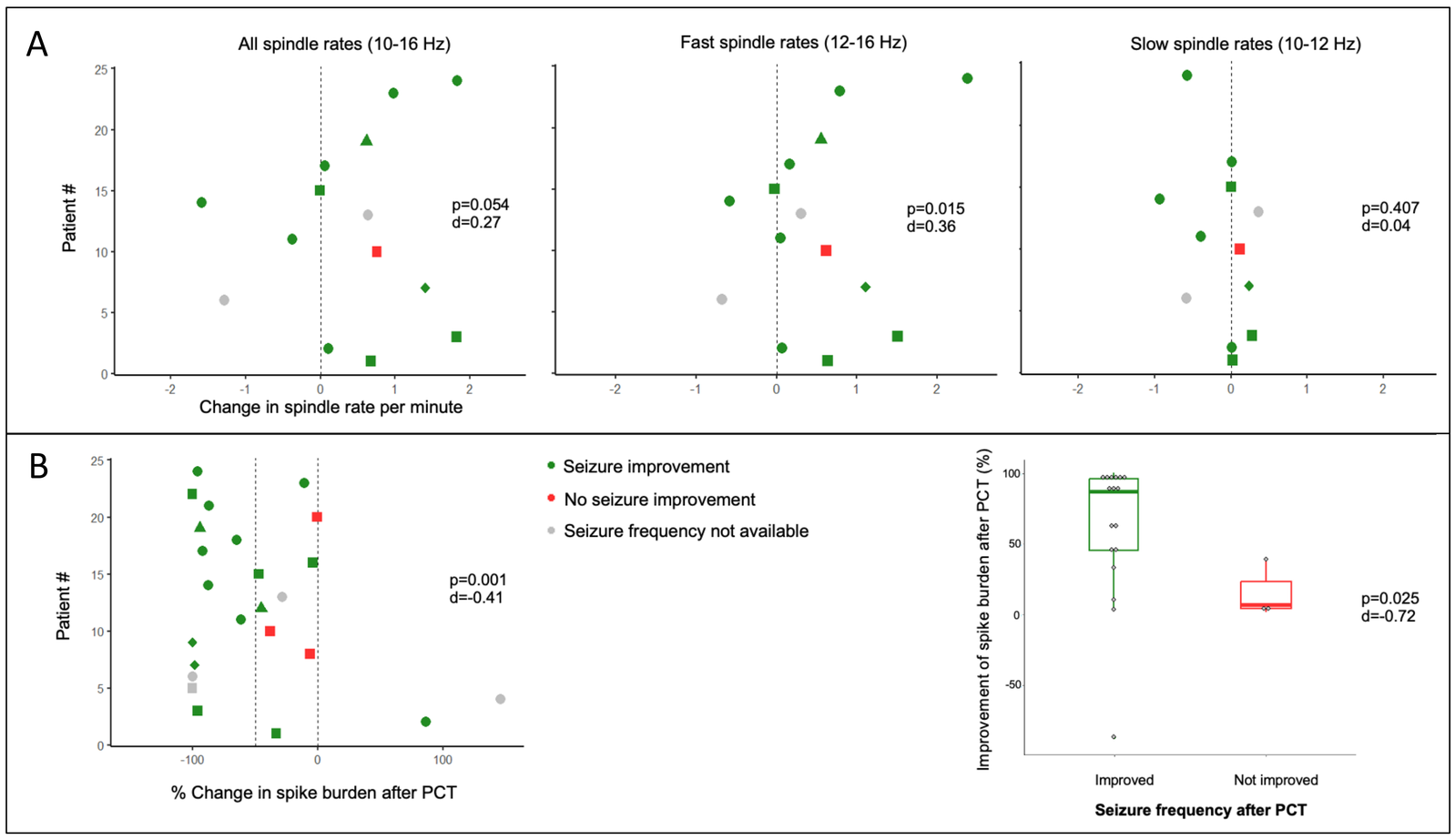

Figure 2. (A) All sleep spindles, fast sleep spindle rates and slow sleep spindle rates presented in change in rate per minute in N2 after PCT. Each square/dot/triangle/diamond represents one patient (generalized epilepsy = square, focal epilepsy = dot, developmental and epileptic encephalopathy syndromes with progressive neurological deterioration = triangle, not classifiable = diamond). (B) Epileptic burden presented as percentage change is significantly reduced after PCT. Patients with improvement of seizure frequency showed significantly higher reduction in spike burden.

CONCLUSION

This is the first study to objectively assess the effects of corticosteroids on sleep physiology expressed by sleep spindles in children with genetic DRE. Sleep spindles play an important role in cognition and learning[44] and fast spindles were found to better predict cognition than slow spindles.[45]

The improvement of spindle activity, and particularly fast spindles, found in our study may therefore coincide with an improvement in cognition and memory. In the interview with parents at the end of PCT, 70.8% reported to have noticed an improvement in cognition and 54.2% in attention/alertness.

In the vast majority of patients, PCT led to an improvement of epileptic activity in the EEG recordings with 11 patients showing a reduction over 50% in the epileptic burden and four patients no longer having an epileptic burden at the end of the treatment.

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