HEADFIRST: Preliminary Results From Home Sleep EEG Testing in Patients With LGS

Jay Pathmanathan[1*]
Franz Fürbass[1*]
Anna Marszalek[1]
Sherry Ann Santarina[1]
P Michelle Fogerson[1]
Tanja S Hellier[2]
Jan Vandenneucker[3]
Matthew S Alkaitis[1]
Jacob Donoghue[1]

1. Beacon Biosignals, Inc., Boston, Massachusetts, United States
2. UCB Inc., Smyrna, Georgia, United States
3. UCB Biopharma SRL, Brussels, Belgium
* These authors contributed equally

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Background

- Sleep pathology is a common comorbidity in patients with Lennox-Gastaut syndrome (LGS), and epileptic abnormalities (including interictal EEG abnormalities and electrographic seizures) are commonly activated in non-REM (NREM) sleep[1].
- Sleep abnormalities have been implicated as contributors to seizure burden and may exacerbate disease comorbidities[2]. In adult LGS patients, sleep disturbances may even contribute to mortality[3].
- Sleep abnormalities are difficult to characterize in LGS patients due to the complexity of obtaining in-lab polysomnographic data.
- Few studies have examined the LGS population[2,4] using brain activity derived sleep staging, and none have examined sleep over multiple nights or used neurotypical sibling controls.
- Prior findings have demonstrated disturbances in sleep cycles and reduced REM sleep.

Objective

Report preliminary findings from the HEADFIRST study, assessing feasibility of at-home longitudinal sleep EEG recording in participants with LGS using the Dreem 3S headband".

Methods

The HEADFIRST Study is an observational cohort study focused on the feasibility of caregivers operating the Dreem 3S EEG Headband (D3S) (no technologist involved) to monitor sleep EEG in their children with developmental and epileptic encephalopathy.

DREEM 3S HEADBAND

- D3S is an FDA 510(k) cleared dry EEG electrode recording device coupled with machine learning (ML) sleep staging algorithms (Figure 1), intended for use by adult patients (without technologist placement) to monitor disturbed sleep
- In this study it is being used off-label as a research use only device to obtain raw EEG data. This report is focused on participants with LGS.

STUDY PARTICIPANTS

- Study participants had a diagnosis of LGS AND [either 2+ seizures per week or diagnosis of global developmental delay requiring 24-hour care]. Demographic details are in Table 1.
- Controls were neurotypical siblings of study participants with LGS, ages 5-18, without neurological diagnoses, on psychoactive treatment, sleep disorders, or developmental delay.
- Recruitment was performed through a partnership with the LGS Foundation
- Caregivers were required to provide consent; study participants provided assent where possible.
- Caretakers placed and operated the D3S on their children (with LGS and any enrolled neurotypical siblings) with minimal training and without intervention of medically trained staff.
- Caregivers were asked to operate the D3S overnight for 5 consecutive nights to obtain EEG data on their children, followed by a 2-night break, and then again for 5 consecutive nights (10 nights over a 2-week period).
- Automated sleep staging, raw EEG from the D3S montage, daily sleep/seizure diaries, and parent reported symptom scales (including PROMIS Parent reported sleep impairment questionnaire) were collected. Statistical comparisons were performed using Welch's t-test of populations with unequal variance. No correction for multiple comparisons was made in this preliminary report.
- All study procedures were approved by WCG IRB (study #1370502)

TABLE 1. POPULATION LEVEL DETAILS

Description	LGS	Control	Total
Participants	9/10	9/9	18/19
Female/Male	3/6	3/6	6/12
Age (mean + standard deviation)	14.1 +/- 4.4 years	13.2 +/- 2.9 years	13.7 +/- 3.8 years
Recordings passing Quality Check (QC)	55	61	116
Recordings (per participant) passing QC	6.1/10	6.8/10	
Hours (per participant) passing QC	55	57	56

Measure	LGS	Control	*P*-value
Total Sleep Time	n=9, mu=479.51, std=93.31, iistd=51.6	n=9, mu=456.6, std=41.96, iistd=63.21	0.52
Wake After Sleep Onset	n=9, mu= 51.71, std=24.66, iistd=26.48	n=9, mu= 21.01, std=10.2, iistd=12.4	**0.0057**
Sleep Onset Latency	n=9, mu= 18.34, std=13.85, iistd= 7.38	n=9, mu= 25.44, std=14.55, iistd=21.04	0.31
NUMBER_AWAKENINGS	n=9, mu= 27.81, std=12.64, iistd= 8.29	n=9, mu= 19.91, std= 6.22, iistd= 5.33	0.12
REM_MINUTES	n=9, mu= 56.77, std=56.39, iistd=18.07	n=9, mu=104.34, std=15.27, iistd=30.16	**0.037**
SLEEP_CYCLES	n=9, mu= 2.63, std=1.52, iistd= 0.64	n=9, mu= 4.65, std= 0.33, iistd= 0.96	**0.0039**

Abbreviations: n = number of subjects; mu = mean value across subjects; std = standard deviation; iistd = intra individual standard deviation (mean of per-subject standard deviations)

Overview

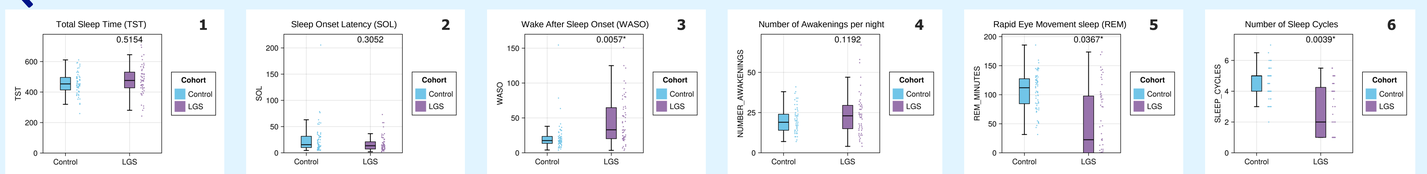
QUESTION

How does sleep differ between patients with Lennox-Gastaut syndrome (LGS) and neurotypical siblings?

INVESTIGATION

Sleep, recorded in participant's natural home environment with the Dreem 3S headband, demonstrated notable similarities and differences between the two populations.

RESULTS



Sleep Parameters: TST – Total Sleep Time (minutes), SOL – Sleep Onset Latency (minutes), WASO – Wake After Sleep Onset (minutes), REM – Rapid Eye Movement Sleep stage

* = statistically significant at p<0.05

CONCLUSIONS

Neither Total Sleep Time nor Sleep Onset Latency was different between the populations. However, LGS participants had significantly greater Wake After Sleep Onset and slightly greater (though not significant) number of awakenings. Marked differences were noted in the amount of REM (with LGS participants having significantly less REM minutes) and sleep cycling patterns (with LGS participants having significantly fewer complete sleep cycles).

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FIGURE 1

The Dreem 3S Headband utilizes dry EEG electrodes and accelerometer data to capture brain and movement activity without technologist setup. Raw EEG and accelerometry data is wirelessly transmitted to Beacon servers, and automatically sleep staged in near real-time. It is designed for patient use at home and is FDA 510(k) cleared for the evaluation of disturbed sleep in adult patients.

EEG Sensors
4 EEG sensors:
A Frontal: F7 / F8
B Ground: FP2
C Occipital: O1 / O2

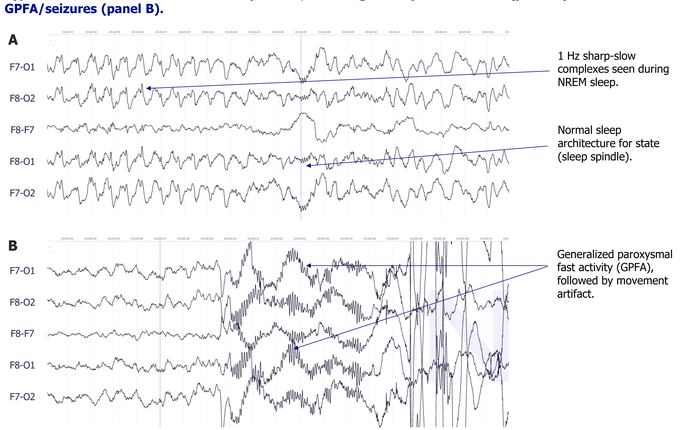
Audio
D Bone conduction speaker for audio output

Accelerometer
E Measures movements, head position during sleep, and respiratory rate (Accelerometer channels are for Research Use Only)

Other
F Power button: on top of the Headband
G Magnetic charging port

FIGURE 2

Typical EEG abnormalities seen in LGS patients, including slow spike-and-wave (panel A) and GPFA/seizures (panel B).



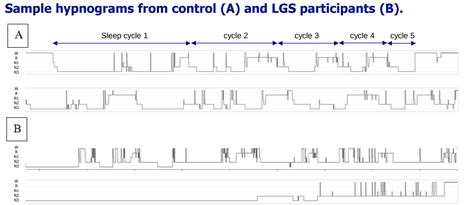
Abbreviations: GPFA – Generalized Paroxysmal Fast Activity, LGS – Lennox-Gastaut Syndrome, NREM – Non-REM sleep state (includes stages 1, 2, and slow-wave sleep), REM – Rapid Eye Movement sleep state, SOL – Sleep Onset Latency (minutes), TST – Total Sleep Time (minutes) , WASO – Wake After Sleep Onset (minutes).

Results

- Preliminary analyses demonstrated marked EEG based sleep state and epileptiform differences between LGS participants and neurotypical controls. As expected, LGS participants (all but one) had characteristic EEG abnormalities of slow (1-2 Hz) spike-wave discharges, sporadic interictal discharges (IEDs), or seizures (including prolonged runs of GPFA) in NREM sleep (Figure 2).
- Sleep architecture also demonstrated marked differences. While total sleep time (TST) and sleep onset latency (SOL) were not significantly different between LGS and control participants (Inset, panels 1 and 2), wake after sleep onset (WASO) time was significantly higher for LGS participants (Inset, panel 3). Number of awakenings was higher in LGS participants, but notably not significant (Inset, panel 4). Overall sleep architecture was also clearly different, with reduced REM duration in the LGS population (Inset, panel 5).
- More apparent was that the distribution of sleep (which normally demonstrates 4-6 periodic cycles of lighter to deeper sleep punctuated with REM intervals) was severely altered in LGS participants (mean of 4.6±0.3 and 2.6±1.5 cycles in neurotypical and LGS participants, respectively, *P*<0.05) (Inset, panel 6). Examples of full night hypnograms are shown in Figure 3 (3A shows 2 control participants, while 3B shows 2 participants with LGS).

FIGURE 3

Sample hypnograms from control (A) and LGS participants (B).



Conclusions

- LGS patients have significant disturbances in sleep architecture, in addition to known epileptic activity in NREM sleep.
- Total sleep time is similar between groups, but LGS participants awoke for more minutes than neurotypical controls.
- Overall sleep architecture was disturbed, with markedly fewer sleep cycles seen in LGS participants than controls.
- LGS participants had a marked reduction in REM sleep relative to sibling controls, which has been previously described.
- Intra-individual variability was high for both controls and LGS participants. WASO effect could have been missed with one night of recording.
- We hypothesize (although have not yet investigated) that nocturnal epileptic events (such as seizures), medication effects (particularly sedating medications that disrupt normal sleep cycling), and disease impacts on the deep frontal, temporal, and hypothalamic circuits underpinning sleep physiology are major contributors to sleep pathology in LGS patients.

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