EEG Spectral Properties and Associated ECG-Based Heart-rate Variability in People With Insomnia Versus Healthy Sleepers

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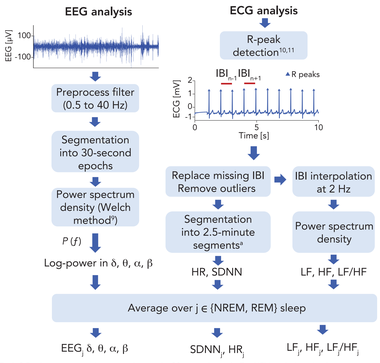
INTRODUCTION

- Insomnia is a sleep disorder characterized by difficulty falling asleep, staying asleep, daytime impairment or distress, or waking up too early and not being able to fall asleep again at least 3 times a week for a minimum period of 1 month, despite adequate opportunity and favorable conditions for sleep.[1]
- Sleep disorders disrupt normal central and autonomic nervous system function during sleep, which may manifest as anomalous electroencephalogram (EEG)/electrocardiogram (ECG) coupling.[2–4]
- People with insomnia have increased EEG α (8–12 Hz) and σ (11–16 Hz) power during rapid eye movement (REM) sleep, and decreased δ (0.5–4Hz) power and increased θ (4–8 Hz), α, β, and σ power during non-REM (NREM) sleep.[5]
- People with insomnia also have notably lower ECG-based heart-rate variability (HRV) during NREM and REM sleep compared with healthy sleepers.[6]
- This study aimed to compare the sleep architecture, central and autonomic nervous system functions, and EEG/ECG coupling of healthy sleepers versus people with insomnia using polysomnography.

Methods

- This study used publicly available, de-identified, polysomnography data from 9 people with insomnia[7,8] and 12 age-matched, healthy sleepers drawn as a subset from an IRB-reviewed, exempt-status study conducted by Sleep Number Corporation.
  - The insomnia cohort was free of neurological disorders and drugs affecting the central nervous system.[8]
  - All insomnia phenotypes were included in the analysis, as the sample size was insufficient to stratify by insomnia phenotype.
- Sleep architecture was characterized for all study participants and the following variables were measured for REM and NREM sleep: spectral EEG power in the δ, θ, α, and β (15–30 Hz) bands; mean heart rate; and mean HRV metrics (**Figure 1**).
  - The β band was included to identify patterns associated with micro-arousals.
  - HRV metrics included standard deviation of normal-to-normal intervals (SDNN), absolute power of the high frequency band (HF, 0.15–0.4 Hz), absolute power of the low frequency band (LF, 0.04–0.15 Hz), and ratio of LF-to-HF (LF/HF) power.
    - Normal-to-normal intervals are defined as R–R intervals after outlier removal.
- Values for EEG power were log-transformed before use in statistical analyses.

FIGURE 1: PROCEDURES FOR THE ANALYSIS OF EEG AND ECG.



[a]Each 2.5-minute segment is centered around a 30-second epoch. For HRV analysis, using longer temporal windows (> 30 s) is recommended.[3]

ECG, electrocardiogram; EEG, electroencephalogram; HF, absolute power of the high frequency band; HR, heart rate; HRV, heart-rate variability; IBI, interbeat intervals; LF, absolute power of the low frequency band; LF/HF, ratio of LF-to-HF power; NREM, non-rapid eye movement; REM, rapid eye movement; SDNN, standard deviation of normal-to-normal (noise-free R–R) intervals.

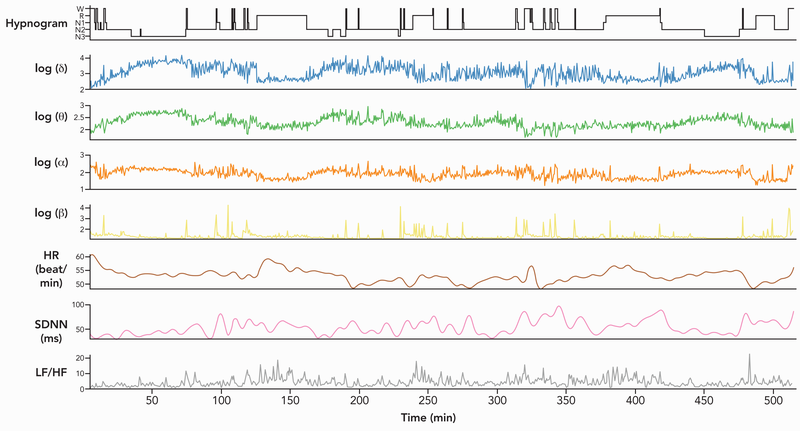
- Values for EEG- and ECG-derived metrics were temporally aligned with their corresponding hypnogram (**Figure 2**).
- A generalized linear model approach was used to assess the degree of coupling between EEG power and ECG-derived metrics in REM and NREM sleep for all study participants using the following equation:

$$\text{Log}\,(\text{EEG}_j\text{B}) \approx \lambda_0 + \lambda_1\text{HR}_j + \lambda_2\text{SDNN}_j + \lambda_3\text{HF} + \lambda_4\text{LF}_j + \lambda_5\frac{\text{LF}_j}{\text{HF}_j}$$

For j ϵ {NREM, REM}, and B ϵ {α, β, δ, θ}, where EEG_jB = EEG power in the frequency band, B, for j sleep.

- Because the range of values differed greatly between model parameters and could have introduced bias, the values for all model parameters were transformed into Z-scores.
- Group differences were tested using the Mann-Whitney U test for all parameters except for gender, which was tested by Z-test.

FIGURE 2: TEMPORAL ALIGNMENT OF EEG- AND ECG-DERIVED METRICS DURING A SLEEP SESSION.



Example alignment for a 46-year-old male healthy sleeper (AHI = 0).

ECG, electrocardiogram; EEG, electroencephalogram; HR, heart rate; LF/HF, ratio of LF-to-HF power; SDNN, standard deviation of normal-to-normal (noise-free R–R) intervals.

Results

- The cohorts were similar in demographic characteristics, baseline sleep architecture, and cardiovascular parameters during sleep (**Table 1**).

TABLE 1. DEMOGRAPHIC, SLEEP ARCHITECTURE, AND CARDIOVASCULAR ATTRIBUTES OF THE STUDY COHORT.

Parameter	Healthy cohort (n = 12)	Insomnia cohort (n = 9)	*P*-value[a]
Age (years) mean ± SD	54.4 ± 4.1	60.9 ± 10.5	0.07
Males, n (%)	5 (41.7)	4 (44.4)	0.70[b]
Sleep metrics (min) mean ± SD			
Sleep latency	45.9 ± 38.2	96.7 ± 125.4	0.67
Total sleep time	362.4 ± 20.6	342.9 ± 77.4	0.75
NREM	276.2 ± 25.3	221.3 ± 73.1	0.15
REM	66.7 ± 26.4	100.1 ± 40.1	0.08
Wake after sleep onset	66.6 ± 26.8	73.8 ± 61.7	0.75
Cardiovascular metrics, mean ± SD			
HR (beats/min)			
NREM	67.6 ± 9.6	66.3 ± 7.3	0.70
REM	69.2 ± 9.9	67.1 ± 7.6	0.54
SDNN (ms)			
NREM	42.6 ± 16.1	46.6 ± 22.8	0.86
REM	47.9 ± 17.5	51.9 ± 32.3	0.94
LF (ms^2)			
NREM	0.2 ± 0.1	0.3 ± 0.3	0.80
REM	0.2 ± 0.1	0.4 ± 0.4	0.70
HF (ms^2)			
NREM	0.1 ± 0.2	0.2 ± 0.3	0.30
REM	0.1 ± 0.2	0.3 ± 0.4	0.22
LF/HF			
NREM	4.1 ± 2.7	2.6 ± 1.2	0.34
REM	4.7 ± 2.9	2.8 ± 1.1	0.11

[a]Mann-Whitney U test unless otherwise indicated; [b]Z-test.

HF, absolute power of the high frequency band; HR, heart rate; LF, absolute power of the low frequency band; LF/HF, ratio of LF-to-HF power; NREM, non-rapid eye movement; REM, rapid eye movement; SD, standard deviation; SDNN, standard deviation of normal-to-normal (noise-free R–R) intervals.

- EEG power was significantly higher for healthy sleepers across all bands (all $P \leq 0.01$), so EEG values for each band were normalized by power in each band divided by total power.
- After normalization, healthy sleepers had significantly higher NREM θ power versus people with insomnia ($P = 0.005$). For all other bands, the power results were not significantly different (**Table 2**).

TABLE 2. COMPARISON OF HEALTHY SLEEPER COHORT VS THOSE WITH INSOMNIA FOR EACH EEG BAND, NORMALIZED FOR TOTAL POWER.

Parameter (mean ± SD)	Healthy cohort (n = 12)	Insomnia cohort (n = 9)	*P*-value[a]
δ power			
NREM	0.34 ± 0.02	0.36 ± 0.03	0.11
REM	0.32 ± 0.02	0.35 ± 0.04	0.06
θ power			
NREM	0.26 ± 0.01	0.24 ± 0.01	< 0.01
REM	0.26 ± 0.01	0.25 ± 0.01	0.08
α power			
NREM	0.23 ± 0.01	0.21 ± 0.02	0.06
REM	0.22 ± 0.01	0.21 ± 0.03	0.13
β power			
NREM	0.17 ± 0.01	0.18 ± 0.02	0.17
REM	0.21 ± 0.03	0.19 ± 0.04	0.29

[a]Mann-Whitney U test.

EEG, electroencephalogram; NREM, non-rapid eye movement; REM, rapid eye movement; SD, standard deviation.

- Generalized linear model analysis for EEG/ECG coupling revealed that HR, SDNN, HF, LF, and the LF/HF ratio were predictors of EEG α power during NREM sleep in people with insomnia, as shown in the following equation (adjusted $R^2 = 0.705$, $P = 0.113$).

$$\text{Log}\,\text{EEG}_{\text{NREM}}\alpha \approx \lambda_1\text{HR}_{\text{NREM}} + \lambda_2\text{SDNN}_{\text{NREM}} + \lambda_3\text{HF}_{\text{NREM}} + \lambda_4\text{LF}_{\text{NREM}} + \lambda_5\frac{\text{LF}_{\text{NREM}}}{\text{HF}_{\text{NREM}}}$$

- Notably, HF and LF/HF decreased, and LF increased, with increasing α power.
- A second generalized linear model analysis was performed to account for collinearities and interactions, which significantly increased model predictability (adjusted $R^2 = 0.974$, $P = 0.02$; **Table 3**).

TABLE 3. THE MODEL FOR NREM EEG-α POWER IN PATIENTS WTIH INSOMNIA, AFTER CONTROLLING FOR COLLINEARITIES AND INTERACTIONS.

Parameter	Coefficient	*P*-value
Intercept	−1.25	0.03
HR_{NREM}	0.15	0.64
$\text{SDNN}_{\text{NREM}}$	4.39	0.02
HF_{NREM}	−10.49	0.01
LF_{NREM}	2.97	0.02
$\text{LF}_{\text{NREM}}/\text{HF}_{\text{NREM}}$	−1.97	0.01
$\text{SDNN}_{\text{NREM}}$: $\text{LF}_{\text{NREM}}/\text{HF}_{\text{NREM}}$	−2.79	0.03

EEG, electroencephalogram; HF, absolute power of the high frequency band; HR, heart rate; LF, absolute power of the low frequency band; LF/HF, ratio of LF-to-HF power; NREM, non-rapid eye movement; SDNN, standard deviation of normal-to-normal (noise-free R–R) intervals.

- These results show that NREM in healthy sleepers is associated with low α power—ie, low central nervous system activity—and high HF, indicating high parasympathetic autonomic nervous system activity.
- A limitation of this study was the small sample size, which may have led to statistical underpowering.

Conclusions

- In our study, we observed significantly lower NREM θ power in the insomnia group compared with healthy sleepers. These results may indicate challenges in falling asleep, as the increase in NREM θ power is a hallmark of the hypnagogic (falling asleep) process.[12]
- We also observed that α power in NREM, likely a marker of restlessness,[13] negatively correlated with HF—reflecting parasympathetic activity—and positively correlated with LF, reflecting baroreflex activity.[14]
- These results suggest that, in people with insomnia, the parasympathetic dominance in NREM sleep is challenged by higher α power, which may decrease sleep quality.
- Furthermore, these results are consistent with previous research noting associations between α power and micro-arousal activity during sleep.[13]
- Adding the interaction between the SDNN time-domain HRV metric and LF/HF frequency-domain HRV metric significantly increased adjusted R^2.
- Further research with a larger population is needed to confirm these results.

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