

EEG Power During Waking and NREM Sleep in Primary Insomnia

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Objective: Pathophysiological models of insomnia invoke the concept of 24-hour hyperarousal, which could lead to symptoms and physiological findings during waking and sleep. We hypothesized that this arousal could be seen in the waking electroencephalogram (EEG) of individuals with primary insomnia (PI), and that waking EEG power would correlate with non-REM (NREM) EEG.

Methods: Subjects included 50 PI and 32 good sleeper controls (GSC). Five minutes of eyes closed waking EEG were collected at subjects' usual bedtimes, followed by polysomnography (PSG) at habitual sleep times. An automated algorithm and visual editing were used to remove artifacts from waking and sleep EEGs, followed by power spectral analysis to estimate power from 0.5–32 Hz.

Results: We did not find significant differences in waking or NREM EEG spectral power of PI and GSC. Significant

correlations between waking and NREM sleep power were observed across all frequency bands in the PI group and in most frequency bands in the GSC group.

Conclusions: The absence of significant differences between groups in waking or NREM EEG power suggests that our sample was not characterized by a high degree of cortical arousal. The consistent correlations between waking and NREM EEG power suggest that, in samples with elevated NREM EEG beta activity, waking EEG power may show a similar pattern.

Keywords: Insomnia, EEG, NREM sleep, wakefulness, spectral analysis

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Up to one-third of adults in the US complain of problems with sleep, and approximately 10% to 15% meet criteria for insomnia disorder.^{1,2} Primary insomnia, a disorder characterized by difficulty falling asleep, staying asleep, or early awakening without significant comorbid psychiatric or physical illness, has long been used as a model to study the pathophysiology of insomnia.³ Multiple studies have demonstrated that insomnia is associated with physiological markers of elevated arousal during both wakefulness and sleep, suggesting that 24-hour hyperarousal may be a defining feature of this condition.^{4,5} The 24-hour hyperarousal model has been supported by data including increased whole-body metabolic rate during waking and sleep, increased ACTH and cortisol secretion before and during early sleep, and elevated heart rate and beta frequency spectral power during non-REM (NREM) sleep.⁵⁻⁹ Impaired cognitive performance may also be related to hyperarousal and sleep disruption in insomnia.¹⁰ Physiological measures of hyperarousal or stress, such as HPA axis activation with increased cortisol secretion, may constitute one mechanism by which insomnia is a risk factor for development of depression associated with increased stress.¹¹⁻¹³

Multiple studies have looked at quantitative electroencephalogram (EEG) as a marker of arousal during sleep in individuals with insomnia. One of the earliest studies identified a slower increase and reduced levels of power in all frequency bands below beta frequency during NREM, coupled with increased

BRIEF SUMMARY

Current Knowledge/Study Rationale: Chronic insomnia is often considered to be a disorder of 24-hour hyperarousal, which may be manifest as elevated high frequency EEG during the sleep EEG. The present study examined whether the waking EEG shows elevated high-frequency activity in chronic insomnia compared to good sleepers, and whether EEG power in different frequency bands correlates between waking and NREM.

Study Impact: Although we did not find elevated high frequency in insomnia patients during waking or NREM sleep, we did find strong correlations in EEG power across waking and NREM states. This suggests that the waking EEG may provide a simple method to identify individuals with particular NREM EEG characteristics.

spectral power in the beta frequency bands.¹⁴ This finding of elevated beta frequency spectral power in sleep has been documented in many other studies.^{8,15,16} In a study done by our own group looking at NREM periods and sex differences in EEG spectral analysis in primary insomnia, we found increased beta power in the first NREM period among women with primary insomnia.¹⁷

Daytime symptoms are another component of primary insomnia, and one of the main reasons why patients seek care.¹⁸ Although symptoms of fatigue and tiredness have long been associated with insomnia, studies of physiological sleepiness typically show increased alertness, at least in younger and middle-aged adults with insomnia.^{11,19,20} Although less

consistently observed, alterations in cognitive functioning or brain activation during task performance have also been noted in insomnia.⁹ In keeping with the 24 hour hyperarousal model of insomnia, indices of heightened arousal may also be detectable during waking EEG using spectral power analysis. In one study looking at EEG during the sleep onset period, i.e., just before and after sleep onset, higher beta power was observed in insomnia patients compared to good sleeper controls, supporting the hypothesis that hyperarousal may also be evident during wakefulness.²¹ Thus, symptoms of arousal and altered brain activation are consistent with the 24-hour hyperarousal theory of insomnia.

Quantitative analysis of the waking EEG could plausibly provide additional evidence of increased arousal in insomnia. Waking EEG spectral power has been studied in other patient populations to examine correlations with specific symptoms. For instance, in patients with obstructive sleep apnea, the correlation between waking EEG spectral power and daytime sleepiness has been examined, with conflicting results.^{22,23} Waking EEG has also been examined as an instrument to predict severity of premenstrual syndrome, again with inconclusive results.²⁴ In a study by Buckelew and colleagues examining good versus poor sleepers, theta suppression was noted in 70% of the good sleepers as opposed to 20% of the poor sleepers.²⁵ While this study included college students rather than insomnia patients per se, the findings suggest that the hyperaroused state of primary insomnia may be captured in waking EEG. Furthermore, a study in healthy young adults showed a correlation between waking and sleeping spectral power, which leads to the expectation that the waking EEG of insomnia patients should display signs of hyperarousal as seen in the sleeping EEG spectral power demonstrated by many studies.²⁶ Another potential advantage of studying the waking EEG is that its frequency characteristics are highly heritable.²⁷ Because waking EEG data collection is simpler and less time-consuming than polysomnography (PSG), it could aid the study of insomnia genetics.

The present study includes secondary data analyses of EEG data from two studies of primary insomnia (PI) and good sleeper controls (GSC) (MH024652). Based on the previous observations of increased beta power during sleep in insomnia, and correlations between wake and sleep EEG in healthy samples, we hypothesized that PI would show increased high-frequency power during waking EEG compared to good sleep controls. Given previous studies of night-to-night stability of EEG power in healthy young adults,²⁸ and apparent genetic determination of an individual's spectral profile, we also hypothesized that the spectral characteristics of the waking EEG in PI group would correlate with those of the NREM.

METHODS

This study constituted a secondary data analysis of waking and NREM data collected in two studies of mood, arousal, and functional neuroanatomy of sleep in adults with PI and GSC.^{18,19} The studies were approved by the University of Pittsburgh Institutional Review Board. Written informed consent was obtained from all subjects prior to enrollment. Participants underwent an initial eligibility screening, completed a set of self-reported retrospective symptoms ratings, a one-week home evaluation

including sleep diary and daily symptom ratings, multiple PSG studies, and standardized waking EEG studies.

Participants included 82 men and women between the ages of 20-50. Demographic and clinical characteristics are displayed in **Table 1**. Participants were recruited through media advertisements, word of mouth, and clinical referrals. All participants first underwent medical, substance, and medication history taking, standard physical exam, routine blood work, and urine drug screen. The Structured Clinical Interview for DSM-IV (SCID) was used to diagnose psychiatric disorder, and sleep history was elicited with a structured interview and questionnaires.^{29,30} Inclusion criteria for the GSC group included ability to speak and understand English and Pittsburgh Sleep Quality Index (PSQI) score ≤ 5 . The PI group met the same inclusion criteria and also were required to have a current diagnosis of primary insomnia according to DSM-IV criteria (difficulty initiating or maintaining sleep with associated daytime symptoms for at least one month, without other comorbid psychiatric or physical condition as an obvious cause)³ and a PSQI score > 5 .³¹ These criteria were used to select a broad sample of primary insomnia patients. Exclusion criteria for both groups included significant or unstable medical condition, current major psychiatric or substance use disorder, substance use disorder in the past 6 months, current use of medications known to affect sleep, including benzodiazepine receptor agonists, antidepressant medications, and over-the-counter drugs; coffee consumption > 4 standard (6-ounce) cups in 24 h; and alcohol consumption > 14 drinks per week. Participants refrained from any alcohol on the days/nights of sleep studies, but were permitted to continue their usual caffeine consumption, in order to avoid withdrawal symptoms. The amount of self-reported alcohol and caffeinated drinks revealed no differences between the two groups (Alcohol: GSC 0.4 [SD 0.6] drinks per day, PI 0.3 [SD 0.4] drinks per day; Caffeine: GSC 1.2 [SD 1.0] drinks per day, PI 1.2 [SD 1.2] drink per day). Specific exclusion criteria for the PI group included any major psychiatric disorder within the last 6 months, and for the GSC group, any history of major psychiatric disorder or primary insomnia. Obstructive sleep apnea and periodic limb movement disorder were excluded using a criterion of apnea-hypopnea index > 15 and periodic limb movement arousal index > 20 on one night of screening polysomnography. No participants were taking psychotropic medications at the time of the study.

Participants completed a set of self-reported symptom ratings, discussed below. They then had a one-week in-home evaluation during which they completed the Pittsburgh Sleep Diary³² for the week, daily ratings of mood and arousal,¹⁸ and ≥ 3 nights of PSG recordings. The Pittsburgh Sleep Diary included bedtime and wake time records. The outcome variables are time in bed, sleep latency, total sleep time, wake after sleep onset, and sleep efficiency. The PSQI was used to measure sleep quality. The Inventory of Depressive Symptomatology (IDS) Self-Report Version targeted symptoms consistent with major depression, though sleep specific questions were removed for analysis purposes.³³ The Hyperarousal Scale was designed to measure daytime alertness among individuals with insomnia.³⁴ The Epworth Sleepiness Scale (ESS) was used to measure sleepiness as the propensity to doze in 8 specific situations.^{35,36} When the participants were asked to sleep in the laboratory after the initial in-home screening

Table 1—Sample Characteristics

	GSC (N = 32) Mean (SD) or % (N)	PI (N = 50) Mean (SD) or % (N)	t, χ^2 , or F-statistic (df) for group ^a	p-value
Demographic and Clinical Characteristics				
Age	32.7 (9.3)	36.3 (8.9)	-1.72 (80) ^b	0.09
% Female	59.4 (n = 19)	50.0 (n = 25)	0.69 (1) ^c	0.41
Duration of insomnia	—	< 1 year: 3 1-5 years: 18 > 5 years: 29	—	—
Pittsburgh Sleep Quality Index score	2.1 (1.1)	11.7 (3.0)	277.52 (1,78)	< 0.001
Epworth Sleepiness Scale score	4.3 (3.0)	6.6 (3.9) n = 49	5.43 (1,77)	0.02
Inventory of Depressive Symptomatology score (minus sleep items)	2.8 (5.1)	11.9 (7.0)	38.59 (1,78)	< 0.001
Hyperarousal Scale score	23.7 (8.3)	32.9 (8.0)	24.60 (1,78)	< 0.0001
Sleep Diary Variables				
Sleep Quality visual analog scale (0-100)	78.0 (11.3) n = 29	45.3 (13.0) n = 49	112.15 (1,74)	< 0.001
Time Spent Asleep (min)	430.1 (65.7) n = 29	351.8 (66.7) n = 49	19.31 (1,74)	< 0.001
Sleep Latency (min) ^d	11.5 (7.2) n = 29	43.1 (41.1) n = 49	42.66 (1,74)	< 0.001
Awake (min) ^d	4.2 (4.1) n = 29	41.8 (32.0) n = 49	68.54 (1,74)	< 0.001
Sleep Efficiency (%) ^e	96.5 (2.3) n = 29	80.6 (11.6) n = 49	139.08 (1,74)	< 0.001
PSG Variables				
Waking EEG (min)	3.3 (0.8)	3.3 (1.1)	0.19 (1,78)	0.67
NREM Period 1 duration (min)	63.3 (23.2) n = 23	60.7 (19.7) n = 43	0.02 (1,62)	0.88
Whole Night NREM duration (min)	303.3 (29.9) n = 23	290.0 (45.0)	0.97 (1,62)	0.33
Total Sleep Time (min)	414.3 (37.7)	397.8 (62.9)	0.53 (1,78)	0.47
Sleep Latency (min) ^d	16.3 (13.0)	27.5 (42.2)	4.18 (1,78)	0.04
Wakefulness After Sleep Onset (min) ^d	26.0 (24.3)	42.2 (39.4)	3.09 (1,78)	0.08
Sleep Efficiency (%) ^e	91.0 (5.1)	85.4 (12.3)	3.73 (1,78)	0.06

^aANCOVA controlling for age and sex. ^bT-test for age: t-statistic (df) reported. ^cChi-square for sex: χ^2 (df) reported. ^dSQRT(X+1) transformation used in the analyses. Means and standard deviation reported in the original units. ^eLN(101-X) transformation used in the analyses. Means and standard deviation reported in the original units. GSC, good sleeper controls; PI, primary insomnia; SD, standard deviation.

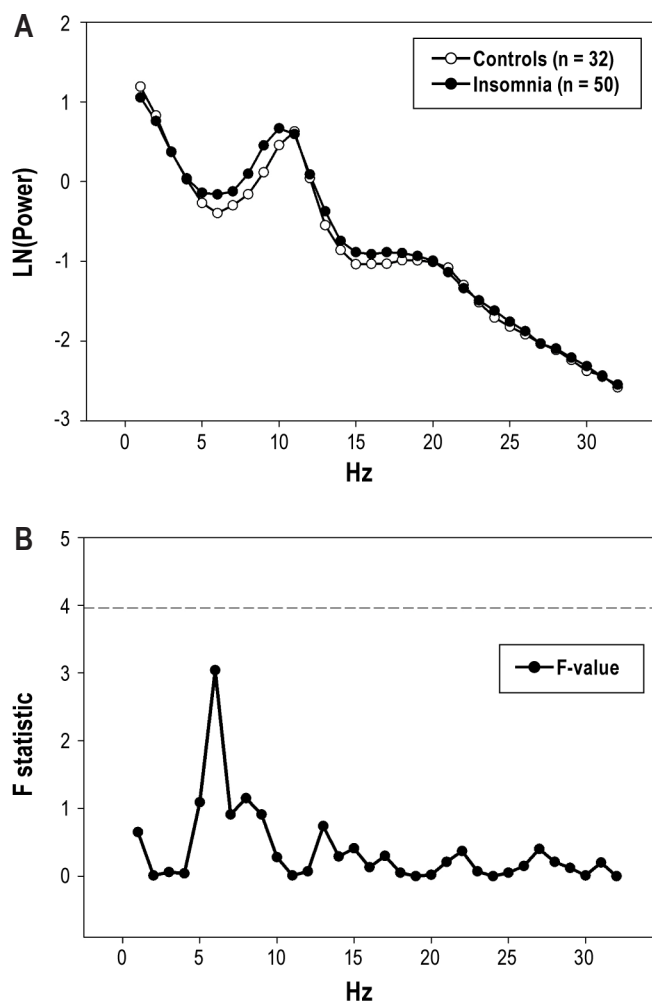
week, they completed the Post-Sleep Evaluation (PSE) which is a locally developed questionnaire with 23 items which focused on the self-evaluation of subjective ratings of the previous night's sleep quality to contrast with PSG measures.

Participants underwent an initial screening evening with PSG recordings followed by 2 nights of baseline PSG for staging and analysis. NREM sleep spectral data were taken from Night 2 unless the recording was not technically adequate, in which case Night 3 data were used. The waking portion of the spectral data was recorded 90-180 minutes prior to habitual bedtime at night on the same night as the PSG study. PSG recordings used standard electrode placement with C3 and C4 EEG leads referenced to A1+A2; right and left electro-oculogram referenced to A1+A2, and bipolar submentalis electromyogram. For the waking EEG with eyes open, participants were asked to stare at a dot on the wall for 5 minutes, minimize blinking, and then they were asked to closed their eyes and fixate on an imaginary dot for 5 minutes, relaxing their eye muscles to minimize

ocular artifacts. Grass Telefactor M15 bipolar Neurodata amplifiers and Stellate Harmonie collection software was used for recording for both waking and sleep EEG.

NREM sleep EEG power spectral analysis was conducted as described in a previous publication, with 50 participants overlapping those in the prior report.¹⁷ Briefly, the PSG was staged in 20-sec epochs according to standard criteria³⁷ prior to the adoption of the new AASM scoring rules. A previously published automated algorithm that uses a moving window threshold was used to eliminate high-frequency EEG artifacts.³⁸ Because the algorithm uses a moving average window, it identifies as artifacts only those epochs that show large and abrupt changes from the surrounding EEG and makes it unlikely to exclude "real" high frequency EEG data. Additional low frequency artifacts such as wakefulness or movement time were visually edited in 4-sec epochs.

Waking EEG data was first edited for high frequency EEG artifact using the same automated algorithm. This was followed

Figure 1

(A) Waking EEG power in primary insomnia and good sleeper control groups. Log-transformed absolute power during eyes-closed waking EEG is shown in 1 Hz bins for participants with primary insomnia (closed circles) and for good sleeper controls (open circles). (B) F Values for eyes closed waking EEG power. F values for log-transformed absolute power during eyes-closed waking EEG, comparing primary Insomnia and Good Sleeper Control groups. ANOVAs were adjusted for age and sex. Critical F value for α of 0.05 is indicated by dashed line.

by visual editing for EKG, muscle, movement, and eye movement artifact. The visual editing standard was established with 5 independent scorers who scored the same 10 records. Overall average κ value for agreement on 4-sec epochs was 0.77 (SD 0.14), and ICC on rejected epochs was 0.97. Using this standard for waking EEG, the waking records were scored twice by 2 independent scorers. In order to ensure adequate EEG data for analysis, only records with > 1 minute of non-artifactual waking EEG were accepted for final analysis.

Statistical Analysis

Descriptive statistics for each cohort were generated to characterize the demographics, clinical, and sleep characteristics of PI and GSC groups. Prior to statistical testing, the data were examined for normality and transformations were used where necessary. Demographics were tested using t-tests

for continuous variables and χ^2 analyses for categorical variables. Analysis of covariance (ANCOVA) was used to test for group differences in clinical and sleep characteristics of the groups covarying for age and sex. EEG spectral power was first compared power within the traditional frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), sigma (12-16 Hz), low beta (16-20 Hz), and high beta (20-32 Hz). Because group differences may not coincide with these traditional frequency bins, we also analyzed the data in individual 1 Hz frequencies, again using ANCOVA. The EEG recordings used for the analysis are the eyes closed portion of the waking EEG, whole night NREM, and NREM period 1 (NREM1). We chose to compare NREM1 separately because NREM1 spectral power was found to have the highest correlation with waking spectral power in a previous study.²⁹

Pearson partial correlation coefficients were used to measure the association between waking and NREM sleep EEG controlling for age. We looked at both whole night and NREM1 correlations within the 6 frequency bins listed above. In addition, we also examined relative power, controlling for total power across all bins between 0.5 to 32 Hz, in each type of analysis.

RESULTS

Table 1 shows demographic, clinical, sleep, and waking EEG data for PI and GSC groups. The PI group was slightly, but not significantly, older than the GSC group. ANCOVA analyses revealed significant difference in PSQI, ESS, IDS, and Hyperarousal Scales, with PI reporting more severe symptoms. All sleep diary variables also indicated significantly worse sleep in the PI group. These are consistent with findings commonly reported in chronic insomnia samples.³⁹ PSG sleep latency was significantly longer in PI than GSC, and differences in wakefulness after sleep onset and sleep efficiency approached, but did not reach, statistical significance. The duration of waking EEG used for analyses did not differ between groups; given the fixed duration of waking EEG recordings, the amount excluded for artifact also did not differ between groups.

Analysis of the 6 traditional frequency bands in waking EEG, NREM1, and whole-night NREM showed no significant differences between the PI and GSC groups (**Table 2**). **Figure 1** displays the EEG power spectrum and F values for individual 1 Hz bins with the waking EEG power spectrum. Only one of these values, at 6 Hz, displays a trend towards a significant difference between the 2 groups. Post hoc analyses of men and women separately showed only one significant difference: the female PI group had significantly greater power in the theta frequency range in the waking EEG ($p = 0.02$).

Table 3 summarizes Pearson correlation coefficients between waking and NREM EEG, adjusted for age. Large correlations were noted for most traditional power bands. In the PI group, significant correlations were observed between waking power and whole-night NREM for all frequency bands. Waking-NREM1 correlations in PI were significant for all bands except alpha and high beta (20-32 Hz). In the GSC group, significant correlations between waking and whole-night NREM EEG were found in all bands except sigma (12-16 Hz). Waking-NREM correlations in GSC were significant for delta and theta bands. For both groups combined, waking EEG power significantly

Table 2—Comparison of EEG spectral power between control and PSC groups controlling for age and sex

Eyes Closed Waking EEG				
Hz Bins	GSC (N = 32) Mean (SD)	PI (N = 50) Mean (SD)	F-value (df = 1,78)	p-value
0.5-4 Hz ^a	2.04 (0.89)	2.03 (1.03)	0.01	0.93
4-8 Hz ^a	0.98 (0.76)	1.21 (0.81)	1.44	0.24
8-12 Hz ^a	2.48 (2.24)	3.08 (3.00)	0.17	0.68
12-16 Hz ^a	0.58 (0.43)	0.65 (0.48)	0.40	0.53
16-20 Hz ^a	0.46 (0.28)	0.51 (0.36)	0.04	0.84
20-32 Hz ^a	0.20 (0.12)	0.21 (0.17)	0.19	0.67
NREM Period 1				
Hz Bins	GSC (N = 23) Mean (SD)	PI (N = 43) Mean (SD)	F-value (df = 1,62)	p-value
0.5-4 Hz ^a	52.88 (37.51)	43.64 (28.67)	0.90	0.35
4-8 Hz ^a	3.99 (1.86)	3.68 (1.91)	0.37	0.55
8-12 Hz ^a	1.81 (1.38)	1.60 (1.14)	0.85	0.36
12-16 Hz ^a	0.79 (0.46)	0.84 (0.49)	0.17	0.68
16-20 Hz ^a	0.12 (0.05)	0.15 (0.08)	1.87	0.18
20-32 Hz ^a	0.04 (0.02)	0.04 (0.02)	1.84	0.18
Whole Night NREM				
Hz Bins	GSC (N = 23) Mean (SD)	PI (N = 43) Mean (SD)	F-value (df = 1,62)	p-value
0.5-4 Hz ^a	32.43 (23.68)	27.80 (16.43)	0.33	0.57
4-8 Hz ^a	2.89 (1.33)	2.74 (1.32)	0.10	0.75
8-12 Hz ^a	1.35 (0.76)	1.38 (0.92)	0.07	0.80
12-16 Hz ^a	0.81 (0.47)	0.81 (0.46)	0.04	0.83
16-20 Hz ^a	0.12 (0.04)	0.14 (0.08)	0.43	0.51
20-32 Hz ^a	0.04 (0.02)	0.04 (0.02)	0.16	0.69

^aLN(X) transformation used in the analyses. Means and standard deviations reported in the original units. GSC, good sleeper controls; PI, primary insomnia; SD, standard deviation.

Table 3—Correlations between waking and NREM EEG

Pearson correlation coefficients for eyes closed waking EEG and NREM period 1 adjusted for age						
Hz Bins	GSC (N = 23)		PI (N = 43)		All Participants (N = 66)	
	r	p	r	p	r	p
0.5-4 Hz ^a	0.57	0.005	0.54	< 0.001	0.54	< 0.001
4-8 Hz ^a	0.62	0.002	0.59	< 0.001	0.59	< 0.001
8-12 Hz ^a	0.27	0.23	0.29	0.07	0.24	0.05
12-16 Hz ^a	-0.02	0.94	0.39	0.01	0.24	0.05
16-20 Hz ^a	0.38	0.08	0.50	< 0.001	0.50	< 0.001
20-32 Hz ^a	0.37	0.09	0.27	0.08	0.29	0.02
Pearson correlation coefficients for eyes closed and whole night NREM adjusted for age						
Hz Bins	GSC (N = 23)		PI (N = 43)		All Participants (N = 66)	
	r	p	r	p	r	p
0.5-4 Hz ^a	0.68	< 0.001	0.54	< 0.001	0.59	< 0.001
4-8 Hz ^a	0.65	0.001	0.56	< 0.001	0.61	< 0.001
8-12 Hz ^a	0.53	0.01	0.31	0.05	0.36	0.003
12-16 Hz ^a	0.00	0.99	0.37	0.02	0.24	0.06
16-20 Hz ^a	0.52	0.01	0.53	< 0.001	0.53	< 0.001
20-32 Hz ^a	0.42	0.05	0.39	0.01	0.40	< 0.001

^aLN(X) transformation used in the analyses. GSC, good sleeper controls; PI, primary insomnia.

correlated with all bands in NREM1 and all bands except sigma in whole-night NREM.

DISCUSSION

These analyses did not show significant differences in waking EEG spectral power between PI and GSC, except for significantly elevated theta in the female PI group. However, we also failed to find group differences in NREM EEG power, as identified in other samples. Strong correlations between waking and sleeping EEG were identified, particularly in the PI group. These correlations suggest that, in samples with greater evidence of EEG hyperarousal during NREM sleep than the current sample, individuals with increased high frequency activity during the NREM EEG would be likely to have increased high-frequency activity during the waking EEG as well.

The absence of differences between groups in NREM beta power suggests that our sample of PI had less significant hyperarousal than those in other published studies, which could also explain the lack of significant beta power activity during waking EEG. Since we found significant wake-NREM correlations for most frequency bands including beta in the PI group, we would expect that samples with increased beta during NREM sleep would also have elevated beta in the waking EEG. Although beta has been suggested as a marker of arousal during NREM, there has been no consensus regarding changes in the waking EEG that would signify hyperarousal. The trend for increased theta power during in the waking EEG of PI vs. GSC suggests differences between the two groups in homeostatic sleep drive or sleepiness, which may be consistent with group differences in ESS score. This may also be consistent with our earlier finding that women with PI have elevated delta during NREM.¹⁷ Thus, at least some individuals with PI may have markers of elevated homeostatic drive during both sleep and wakefulness in addition to, or instead of, hyperarousal. In another recent study of waking EEG, the PI cohort exhibited increased beta but decreased theta during waking, which differs from our data.³⁹ Use of absolute vs. relative EEG power and different electrode derivations in the previous study may contribute to these observed differences. Our PI sample also had lower scores on the Hyperarousal Scale compared to previous studies,^{34,40} a difference that may be reflected in EEG characteristics.

Our findings raise several questions for future investigation. First, it would be important to examine theta and beta power during the waking EEG in a group of insomnia patients with more clearly increased arousal. For instance, individuals with increased beta EEG power during NREM or increased cortisol during sleep may be more likely to have increased beta power during waking EEG as well. Second, our findings raise the question of the significance of increased theta power during wake in patients with PI. In previous studies, increased power in the theta frequency range is associated with decreased alertness.⁴¹ Our sample of PI patients had higher ESS scores than the GSC group, indicating a higher level of self-reported tendency to doze in PI. However, most studies of insomnia show reduced physiological sleepiness with techniques such as the multiple sleep latency test.^{20,42} It is possible that increased theta is a more sensitive objective manifestation of sleepiness

in PI than the MSLT, with its associated demand characteristics. It is also possible that waking EEG theta may better correlate with insomnia patients' subjective sleepiness and fatigue than does the MSLT.

Our study has several limitations. Our sample size was relatively small. The larger number of PI patients may have provided greater power to detect significant correlations in this group, compared to GSC. The sample of waking EEG was short (5 minutes total collected), and it was recorded at a single time of day, which would limit our waking EEG comparison to one period in the day and does not adequately account for diurnal variations in alertness or EEG. The strength of our study is using a standardized waking EEG protocol and data editing and analysis, and our PI sample closely follows the population seen clinically.

In summary, we did not find differences in waking EEG power between PI and GSC. However, the strong correlations between waking and NREM EEG suggest that further exploration of the waking EEG in carefully selected PI samples is warranted.

REFERENCES

1. Leger D, Scheuermaier K, Raffray T, Metlaine A, Choudat D, Guilleminault C. HD-16: a new quality of life instrument specifically designed for insomnia. *Sleep Med* 2005;6:191-8.
2. Ohayon MM. Epidemiology of insomnia: What we know and what we still need to learn. *Sleep Med Rev* 2002;6:97-111.
3. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders (DSM-IV)*. 4th ed. Washington, DC: American Psychiatric Association, 1994.
4. Bonnet MH, Arand DL. Hyperarousal and insomnia. *Sleep Med Rev* 1997;1:97-108.
5. Riemann D, Spiegelhalder K, Feige B, et al. The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Med Rev* 2010;14:19-31.
6. Bonnet MH, Arand DL. 24-hour metabolic rate in insomniacs and matched normal sleepers. *Sleep* 1995;18:581-8.
7. Vgontzas AN, Bixler EO, Lin HM, et al. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications. *J Clin Endocrinol Metab* 2001;86:3787-94.
8. Perlis ML, Merica H, Smith MT, Giles DE. Beta EEG activity and insomnia. *Sleep Med Rev* 2001;5:363-74.
9. Covassin N, De ZM, Sarlo M, De Min TG, Sarasso S, Stegagno L. Cognitive performance and cardiovascular markers of hyperarousal in primary insomnia. *Int J Psychophysiol* 2011;80:79-86.
10. Fortier-Brochu E, Beaulieu-Bonneau S, Ivers H, Morin CM. Insomnia and daytime cognitive performance: a meta-analysis. *Sleep Med Rev* 2012;16:83-94.
11. Hall M, Buysse DJ, Nowell PD, et al. Symptoms of stress and depression as correlates of sleep in primary insomnia. *Psychosom Med* 2000;62:227-30.
12. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord* 2011;135:10-9.
13. Szklo-Coxe M, Young T, Peppard PE, Finn LA, Benca RM. Prospective associations of insomnia markers and symptoms with depression. *Am J Epidemiol* 2010;171:709-20.
14. Merica H, Blois R, Gaillard JM. Spectral characteristics of sleep EEG in chronic insomnia. *Eur J Neurosci* 1998;10:1826-34.
15. Perlis ML, Smith MT, Andrews PJ, Off H, Giles DE. Beta/Gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. *Sleep* 2001;24:110-7.
16. Freedman RR. EEG power spectra in sleep-onset insomnia. *Electroencephalogr Clin Neurophysiol* 1986;63:408-13.
17. Buysse DJ, Germain A, Hall ML, et al. EEG spectral analysis in primary insomnia: NREM period effects and sex differences. *Sleep* 2008;31:1673-82.
18. Harvey AG, Tang NK, Browning L. Cognitive approaches to insomnia. *Clin Psychol Rev* 2005;25:593-611.
19. Buysse DJ, Thompson W, Scott J, et al. Daytime symptoms in primary insomnia: A prospective analysis using ecological momentary assessment. *Sleep Med* 2007;8:198-208.

20. Stepanski E, Zorick F, Roehrs T, Young D, Roth T. Daytime alertness in patients with chronic insomnia compared with asymptomatic control subjects. *Sleep* 1988;11:54-60.
21. Lamarche CH, Ogilvie RD. Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. *Sleep* 1997;20:724-33.
22. Grenache J, Krieger J, Erhardt C, et al. EEG spectral power and sleepiness during 24 h of sustained wakefulness in patients with obstructive sleep apnea syndrome. *Clin Neurophysiol* 2008;119:418-28.
23. Sforza E, Grandin S, Jouy C, Rochat T, Ibanez V. Is waking electroencephalographic activity a predictor of daytime sleepiness in sleep-related breathing disorders? *Eur Respir J* 2002;19:645-52.
24. Baker FC, Colrain IM. Daytime sleepiness, psychomotor performance, waking EEG spectra and evoked potentials in women with severe premenstrual syndrome. *J Sleep Res* 2010;19:214-27.
25. Buckelew SP, DeGood DE, Roberts KD, Butkovic JD, MacKewn AS. Awake EEG dysregulation in good compared to poor sleepers. *Appl Psychophysiol Biofeedback* 2009;34:99-103.
26. Ehlers CL, Kupfer DJ, Buysse DJ, et al. The Pittsburgh study of normal sleep in young adults: Focus on the relationship between waking and sleeping EEG spectral patterns. *Electroencephalogr Clin Neurophysiol* 1998;106:199-205.
27. Finelli LA, Baumann H, Borbély AA, Achermann P. Dual electroencephalogram markers of human sleep homeostasis: correlation between theta activity in waking and slow-wave activity in sleep. *Neuroscience* 2000;101:523-9.
28. Israel B, Buysse DJ, Krafty RT, Begley A, Miewald J, Hall M. Short-term stability of sleep and heart rate variability in good sleepers and patients with insomnia: For some measures, one night is enough. *Sleep* 2012;35:1285-91.
29. First M, Spitzer RL, Gibbon M, Williams JB. *Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition (SCID-I/P)*. Version 2.0 ed. New York: New York State Psychiatric Institute, 1995.
30. First MB, Gibbon M, Spitzer RL, Williams JB. *Structured Clinical Interview for DSM-IV Axis I Disorders SCID I: Clinician version, administration booklet*. Washington, DC: American Psychiatric Press, 1997.
31. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Res* 1989;28:193-213.
32. Monk TH, Reynolds CF, Kupfer DJ, et al. The Pittsburgh Sleep Diary. *J Sleep Res* 1994;3:111-20.
33. Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychol Med* 1996;26:477-86.
34. Regestein QR, Dambrosia J, Hallett M, Murawski B, Paine M. Daytime alertness in patients with primary insomnia. *Am J Psychiatry* 1993;150:1529-34.
35. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 1992;15:376-81.
36. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14:540-5.
37. Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects* NIH Publication 204. Washington, DC: U.S. Government Printing Office, Department of Health Education and Welfare, 1968.
38. Brunner DP, Vasko RC, Detka CS, Monahan JP, Reynolds CF, Kupfer DJ. Muscle artifacts in the sleep EEG: Automated detection and effect on all-night EEG power spectra. *J Sleep Res* 1996;5:155-64.
39. Buysse DJ, Ancoli-Israel S, Edinger JD, Lichstein KL, Morin CM. Recommendations for a standard research assessment of insomnia. *Sleep* 2006;29:1155-73.
40. Wolynczyk-Gmaj D, Szelenberger W. Waking EEG in primary insomnia. *Acta Neurobiol Exp (Wars)* 2011;71:387-92.
41. Aeschbach D. Slow waves and learning: beyond correlations. *Sleep* 2009;32:1253-4.
42. Bonnet MH, Arand DL. Activity, arousal, and the MSLT in patients with insomnia. *Sleep* 2000;23:205-12.

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