

Symptoms of Stress and Depression as Correlates of Sleep in Primary Insomnia

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Objective: Previous studies have not evaluated the clinical correlates of the electroencephalographic spectral profile in patients with insomnia. In the preliminary study described here, we evaluated the extent to which symptoms of stress and depression are associated with subjective sleep complaints and quantitative measures of sleep in individuals with chronic insomnia. **Methods:** Subjects were 14 healthy adults who met criteria for primary insomnia as specified in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*. Measures of stress, depression, and subjective sleep quality were collected before subjects participated in a two-night laboratory sleep series. We hypothesized that elevated symptoms of stress and depression would be associated with subjective sleep complaints and electroencephalographic evidence of hyperarousal during sleep. Hyperarousal during sleep was defined as decreases in delta power and elevations in alpha and beta power throughout non-rapid eye movement sleep, and symptoms of stress were defined as the tendency to experience stress-related intrusive thoughts and the interaction between intrusion tendency and the number of recent stressful events (subjective stress burden). **Results:** A stronger tendency to experience stress-related intrusive thoughts was associated with greater sleep complaints and a trend toward higher beta power, whereas increases in subjective stress burden were associated with decreases in delta power. In addition, elevations in subclinical symptoms of depression were associated with greater sleep complaints and elevations in alpha power. **Conclusions:** Observed relationships among symptoms of stress, depression, subjective sleep complaints, and electroencephalographic power may be relevant to the discrepancy between subjective and objective measures of sleep in patients with insomnia and may be more broadly applicable to sleep complaints in association with stressful life events and major depression. **Key words:** insomnia, stress, depression, electroencephalography, power spectra, arousal.

CNS = central nervous system; DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition; EEG = electroencephalographic; HRSD = Hamilton Rating Scale for Depression; REM = rapid eye movement.

INTRODUCTION

Quantitative EEG studies have consistently reported alterations in EEG power among patients with insomnia in comparison with age-matched, healthy control subjects. Heightened beta activity and attenuated delta power during the sleep onset period are the most reliable alterations, although increases in alpha power have been noted as well (1–3). Merica et al. (4) recently reported that alterations in EEG spectral power among

patients with insomnia are not restricted to the sleep onset period; instead, these differences are seen throughout the night, during both non-REM and REM sleep. The EEG spectral profile of patients with insomnia is consistent with hyperarousal and has generated a lot of interest because it supports the hypothesis that heightened CNS activity, including cortical arousal, plays a role in insomnia (5).

Although it has been suggested that the EEG spectral profile of patients with insomnia is related to clinical correlates of the disorder, previous studies have not investigated these relationships. In the preliminary study reported here, we evaluated symptoms of stress and depression in conjunction with laboratory sleep studies in a sample of adults with chronic primary insomnia. We hypothesized that symptoms of stress and depression were likely correlates of EEG spectral power because each has been independently associated with hyperarousal during sleep and waking (6, 7) and because each is commonly associated with insomnia. Specifically, we hypothesized that the tendency to experience stress-related intrusive thoughts, subjective stress burden, and symptoms of depression would be positively correlated with indices of hyperarousal during sleep, indicated by attenuation of delta power and heightened alpha and beta power. Because subjective sleep complaints are also thought to reflect hyper-

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arousal during sleep (4, 8), we also hypothesized that heightened symptoms of stress and depression would be associated with subjective sleep complaints. Symptoms of stress were operationally defined as the tendency to experience stress-related intrusive thoughts and subjective stress burden. Each of these is more strongly related to sleep than are checklist measures of stressful life events (9, 10).

METHODS

Subjects were 14 adults (9 women and 5 men; mean age, 53 ± 12 years) who met DSM-IV criteria for primary insomnia. Mean duration of insomnia was 17.7 ± 9.9 years. Diagnostic eligibility was determined with a structured sleep disorders interview and the Structured Clinical Interview for DSM-IV Axis I Disorders (11). Sleep laboratory criteria were not used to determine eligibility. Additional eligibility criteria required that subjects be free of major medical or psychiatric illness for 6 months before the study. Although subjects had no current affective or anxiety disorders at the time of the study, six subjects had a history of depression. Subjects were also excluded if they demonstrated significant sleep apnea or periodic limb movements (>10 apneas, hypopneas, or limb movements per hour of sleep) as determined by polysomnography. By the time of the sleep studies, all subjects had discontinued use of all prescription medications that might affect EEG sleep recordings (4 weeks for fluoxetine and 2 weeks for others).

Measures germane to the present report were collected 1 week before baseline sleep studies and commencement of pharmacotherapy, with the exception of sleep diary data, which were collected daily for 2 weeks before the sleep studies. Two variables were used to quantify symptoms of stress to capture the tendency to experience stress-related intrusive thoughts (intrusion tendency) and actual stress levels at the time of sleep studies (subjective stress burden). Intrusion tendency was measured with a modified version of the Impact of Event Scale (12). Subjects were asked to indicate how frequently they generally experience each of seven symptoms of intrusive thoughts after a stressful event. Subjective stress burden was quantified with a summary score, which was calculated as the interaction between intrusion tendency and the number of stressful events that were reported during the 6 months preceding the sleep studies (13). Current symptoms of depression were quantified with the clinician-administered HRSD (14). We used the 14-item HRSD to avoid confounding the HRSD sleep items with study outcomes.

Data from the Pittsburgh Sleep Diary (15) were used to quantify subjective sleep quality, based on daily ratings recorded on a 10-cm visual analog scale. Mean visual analog scale values were calculated for the 2-week period preceding sleep studies, with higher numbers reflecting better sleep quality (scale = 0–100). Laboratory sleep studies included two nights of polysomnography, during which time subjects adhered to their habitual sleep and wake schedules. Polysomnographic data were collected with use of Grass model 78 amplifiers and digitized online at a sampling rate of 256 Hz (12-bit resolution). Sleep records were visually scored in 60-second epochs according to the Pittsburgh version of standard criteria (16), and EEG data (C_3 or C_4 referenced to A_1 – A_2) were decimated to a sampling rate of 128 Hz in preparation for power spectral analysis. Fast Fourier transformation analysis was then used to calculate EEG power spectral densities for consecutive 4-second epochs in 0.25-Hz frequency band widths. A relative artifact threshold detection algorithm, built into the spectral program, was used to identify and eliminate 4-second epochs with muscle artifacts (17). Average absolute power density in the delta (0.5–4.0 Hz), alpha (8.0–12.0 Hz),

and beta (17.0–32.0 Hz) frequency bins were calculated for non-REM sleep during night 2 of the sleep studies; night 1 was considered an adaptation and screening night.

Nonparametric statistics were used in all analyses because of the nonnormal distribution of sleep data and the modest sample size. The influence of age and sex on sleep was evaluated before study hypotheses were tested. Spearman rank-order correlations were then used to evaluate the hypothesis that elevated symptoms of stress and depression would be associated with subjective sleep complaints and CNS hyperarousal as defined by lower absolute delta power and increases in alpha and beta power. A limited number of analyses were specified, *a priori*, to address hypotheses regarding measures of sleep disruption and heightened arousal. The α level was set at 0.05 for all analyses.

RESULTS

Intrusion tendency levels were high (mean = 19.7 ± 4.3), with mean values similar to those of adults seeking treatment for stress disorders (18, 19). Despite high intrusion tendencies, symptoms of depression were low, as shown by the restricted range of depressive symptoms on the 14-item HRSD (range, 2–12; mean = 6.2 ± 3.2). The range of symptoms on the full (17-item) HRSD was 5 to 15. Symptoms of insomnia were evident in poor subjective sleep quality scores (mean = 44.5 ± 16.1) and in the amount of wakefulness after sleep onset as measured by polysomnography (mean = 65.9 ± 59.5 minutes), although sleep latency times were not long on average (mean = 17.1 ± 11.5 minutes). Age and sex were not significant influences on measures of subjective sleep quality and EEG-assessed sleep and were eliminated from further analyses.

Relationships among symptoms of stress, depression, and quantitative measures of sleep are shown in Table 1. Higher subjective stress burden was inversely associated with delta power during non-REM sleep ($p < .01$), and a trend emerged for higher intrusion tendency to be associated with higher absolute beta power during non-REM sleep ($p < .06$). There was also a significant positive correlation between symptoms of depression and alpha power during non-REM sleep ($p < .05$).

As shown in Table 1, higher intrusion tendencies and elevated symptoms of depression were both associated with poorer subjective sleep quality (p values $< .05$). Intrusion tendency and symptoms of depression were not significantly correlated ($\rho = 0.38$, $p < .18$), which suggests that each contributed independently to subjective sleep quality ratings. Subjective stress burden was not a significant correlate of subjective sleep quality ratings.

DISCUSSION

To our knowledge, this is the first study to document relationships among clinical correlates of insom-

TABLE 1. Spearman Rank-Order Correlations Among Symptoms of Stress, Depression, and Sleep

	ρ		
	Intrusion Tendency	Subjective Stress Burden	Symptoms of Depression
Subjective sleep quality			
Diary-based sleep quality	−0.58 ^a	0.37	−0.65 ^a
Average absolute power during non-REM sleep			
Delta (0.5–4.0 Hz)	0.19	−0.73 ^b	0.48
Alpha (8.0–12.0 Hz)	0.06	−0.47	0.68 ^a
Beta (17.0–32.0 Hz)	0.53 ^c	−0.20	0.14

^a $p < .05$.^b $p < .01$.^c $p = .06$.

nia and quantitative EEG measures in patients with insomnia. Study results support the hypothesis that symptoms of stress and depression are significant correlates of hyperarousal throughout non-REM sleep in insomnia, as defined by attenuated delta power and heightened alpha power. Elevated levels of subjective stress and heightened intrusion tendencies were associated with attenuated delta power and a trend for heightened beta power, respectively, whereas subclinical levels of depression were significantly associated with heightened alpha power. Elevated intrusion tendencies and increased symptoms of subclinical depression were significantly associated with poorer subjective sleep quality.

Our results are consistent with neurocognitive and neurophysiological models of insomnia, which have proposed that hyperarousal during sleep contributes to the experience of disturbed sleep but may not be reflected in traditional EEG-assessed measures of sleep (3, 8). The observed link between symptoms of stress, depression, CNS hyperarousal, and subjective sleep complaints is intriguing because it addresses the commonly reported paradoxical discrepancy between subjective and objective measures of sleep in patients with insomnia. Heightened CNS arousal in patients with insomnia is thought to reflect heightened wakelike mentation and/or information and sensory processing, which is experienced as wakefulness (3, 8). Thus, alterations in the phenomenology of sleep may result in subjective perceptions of shortened or nonrestorative sleep that are out of proportion to the degree of sleep disruption identified by traditional visual sleep stage scoring.

Linear relationships among psychological factors and quantitative, as well as subjective, measures of sleep are relevant to the etiology of insomnia and to the pathophysiology of affective disorders, such as major depression. Our results show that stress and subclinical symptoms of depression are significant

correlates of sleep, even in the absence of current psychiatric disorders and despite a restricted range of depressive symptomatology. This suggests that the degree of associated distress, as opposed to a dichotomous distinction based on presence or absence, may be what distinguishes a diagnosis of primary insomnia from a diagnosis of insomnia related to another mental disorder (20). That increasing levels of distress were associated with increasing severity of sleep disruptions also suggests one avenue by which insomnia behaves as a risk factor for depression (21). As a proxy measure for escalating levels of distress, chronic insomnia may be used as a vulnerability marker for risk of depression. It is important to recognize, however, that distress and insomnia are most likely characterized by a bidirectional relationship, with distress interfering with sleep and sleep disruptions eliciting distress. Thus, a linear association among psychological factors and sleep does not necessarily imply that sleep acts only as a signal, and plays no causal role, in the distress-depression relationship.

Relationships among distress and sleep may also be broadly germane to complaints of poor and nonrestorative sleep in association with stressful life events or major depression. For example, subjective sleep complaints in association with stressful life events or major depression may be a function of heightened fast frequency activity and attenuated delta power during sleep, as opposed to a general response set that is related to a negative affective bias. Although previous studies have not evaluated relationships among stress and quantitative EEG measures during sleep, power spectral findings consistent with arousal during sleep have been observed in patients with major depression (22). In future studies, hyperarousal during the period of sleep onset and throughout the night may prove to be an important link between distress and sleep, regardless of whether distress is related to stressful life events, major depression, or insomnia.

Limitations of the present study include the cross-sectional nature of the data and the modest sample size. Strengths of the study include the use of quantitative measures of stress and depression in association with quantitative measures of EEG sleep and the use of a well-defined sample of adults with chronic primary insomnia. Although study hypotheses were advanced on the basis of previous theoretical and empirical work, replication of results in larger, prospective studies is needed to allow more definitive conclusions regarding relationships among symptoms of stress, depression, subjective sleep complaints, and EEG measures of hyperarousal during sleep. Finally, it is important to note that measures of stress may advance our understanding of sleep in insomnia; likewise, stress research may benefit from the use of quantitative measures of EEG-assessed sleep.

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REFERENCES

1. Freedman RR. EEG power spectra in sleep-onset insomnia. *Electroencephalogr Clin Neurophysiol* 1986;63:408–13.
2. Lamarche CH, Ogilvie RD. Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. *Sleep* 1997;20:724–33.
3. Merica H, Gaillard JM. The EEG of the sleep onset period in insomnia: a discriminant analysis. *Physiol Behav* 1992;52:199–204.
4. Merica H, Blois R, Gaillard JM. Spectral characteristics of sleep EEG in chronic insomnia. *Eur J Neurosci* 1998;10:1826–34.
5. Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. *Sleep* 1995;18:581–8.
6. Davidson LM, Fleming R, Baum A. Chronic stress, catecholamines, and sleep disturbance at Three Mile Island. *J Hum Stress* 1987;13:75–83.
7. Armitage R. Microarchitectural findings in sleep EEG in depression: diagnostic implications [editorial]. *Biol Psychiatry* 1995;37:72–84.
8. Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: the behavioural model and a neurocognitive perspective [review]. *J Sleep Res* 1997;6:179–88.
9. Hall M, Buysse DJ, Dew MA, Prigerson HG, Kupfer DJ, Reynolds CF. Intrusive thoughts and avoidance behaviors are associated with sleep disturbances in bereavement-related depression. *Depress Anxiety* 1997;6:106–12.
10. Paulsen VM, Shaver JL. Stress, support, psychological states and sleep. *Soc Sci Med* 1991;32:1237–43.
11. First M, Spitzer RL, Gibbon M, Williams JBW. 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.
12. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med* 1979;41:209–18.
13. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. *J Psychosom Res* 1967;11:213–8.
14. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62.
15. Monk TH, Reynolds CF, Kupfer DJ, Buysse DJ, Coble PA, Hayes AJ, Machen MA, Petrie SR, Ritenour AM. The Pittsburgh Sleep Diary. *J Sleep Res* 1994;3:111–20.
16. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Washington DC: Dept. of Health Education and Welfare (US); 1968. NIH Publication No. 204.
17. 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.
18. Gavish M, Laor N, Bidder M, Fisher D, Fonia O, Muller U, Reiss A, Wolmer L, Karp L, Weizman R. Altered platelet peripheral-type benzodiazepine receptor in posttraumatic stress disorder. *Neuropsychopharmacology* 1996;14:181–6.
19. Horowitz MJ, Weiss DS, Kaltreider N, Krupnick J, Marmar C, Wilner N, DeWitt K. Reactions to the death of a parent. *J Nerv Ment Dis* 1984;172:383–92.
20. DSM-IV. Diagnostic and statistical manual of mental disorders. 4th ed. Washington DC: American Psychiatric Association; 1994.
21. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry* 1996;39:411–8.
22. Pollock VE, Schneider LS. Quantitative, waking EEG research on depression. *Biol Psychiatry* 1990;27:757–80.