Vulnerability to Stress-related Sleep Disturbance and Hyperarousal

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Study Objectives: To determine the presence of a hypothesized trait vulnerability to sleep disturbance and hyperarousal.

Design: Polysomnographic assessment of sleep in response to stress during a first night in the laboratory and subsequent physiologic arousal.

Participants: One hundred and four individuals (46% men, mean age = 40.4 ± 12.9 years) drawn from a population-based sample.

Interventions: Individuals were exposed to a first night in the laboratory.

Measurements and Results: Participants completed a Likert-scale questionnaire, consisting of 27 items, that assesses sleep disturbance in response to commonly experienced stressful situations. Factor analytic techniques identified a single 9-item factor that was representative of the construct of "stress-related" vulnerability to sleep disturbance. Reliability of the resulting 9-item scale was high (Cronbach's α = .83). Individuals with higher scores on this scale, the Ford Insomnia Response to Stress Test (FIRST; median split), had a lower sleep efficiency (P = .001), as well as an increased latency to stage 1 sleep (P = .001) and persistent sleep (P = .002) on the first night of nocturnal polysomnography. Moreover, these high-scoring individuals showed increased arousal as evidenced by an elevated sleep latency on the Multiple Sleep Latency Test compared to individuals with low FIRST scores. Importantly, after controlling for current and past insomnia, the differences between individuals scoring high and low on the FIRST in terms of nocturnal sleep and daytime arousal remained significant. Other stages of sleep (stage 2, slow-wave, and rapid eye movement sleep) were not different between the groups.

Conclusions: These results showing a relationship between FIRST scores and nocturnal polysomnography and Multiple Sleep Latency Test scores have 3 potential implications: (1) the data demonstrate a characteristic that relates to vulnerability to stress-related sleep disturbance as manifested by a first night in the laboratory; (2) the elevated latencies on the Multiple Sleep Latency Test in these individuals, despite significantly disturbed sleep, support the notion of physiologic hyperarousal in these individuals and suggests they may be predisposed to developing chronic primary insomnia; and (3) the vulnerability identified may underlie vulnerability to transient sleep disturbance associated with other sleep-disruptive factors.

Key Words: Insomnia, predisposition, population-based, first-night effect, hyperarousal, sleep disturbance, Multiple Sleep Latency Test, arousal

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INTRODUCTION

INSOMNIA IS THE MOST PREVALENT SLEEP PROBLEM, AFFECTING 10% TO 15% OF THE GENERAL POPULATION. In population-based studies, severe insomnia has been shown to last for a median of 4 years,[1] and 44% of individuals with severe insomnia continue to have their sleep disturbance 10 years later.[2] In addition to disturbed sleep, insomnia has a significant negative impact on an individual's quality of life. After controlling for comorbid illnesses, individuals with insomnia report significantly impaired work performance,[3] lower physical and social functioning,[4] and an overall quality of life comparable to that of individuals with chronic conditions such as congestive heart failure and major depressive disorder.[5] Among the most significant findings in recent years is that insomnia is associated with a subsequent 2- to 5-fold increased risk for major depressive disorder[6-9] and that depressed patients with insomnia have increased rates of suicidal behavior in comparison to depressed patients without sleep disturbance.[10] The overall economic cost of insomnia related to lost productivity, work-related accidents, and absenteeism has been estimated at between $77.05 billion and $92.13 billion dollars per year.[11]

To date, insomnia research has focused mainly on primary insomnia. The *Diagnostic and Statistical Manual-IV* (DSM-IV) diagnostic classification defines primary insomnia as difficulty initiating or maintaining sleep, or nonrestorative sleep, persisting more than 1 month, associated with impairment in daytime function, for which there is no identifiable cause. Models of primary insomnia generally conceptualize the pathophysiology of this disorder from the context of a precipitating event superimposed upon a predisposition and subsequent maintaining factors.[12] However, it is important to recognize that although current diagnostic systems such as the DSM-IV emphasize the presence of "easily disturbed sleep" prior to the development of insomnia as a predisposition or vulnerability to insomnia, the identification of such a predisposition and its link to sleep disturbance and subsequent risk for primary insomnia has not been demonstrated.

Individual differences in the vulnerability to sleep disturbance may constitute a continuum from vulnerability to transient or episodic insomnia through overt chronic primary insomnia. Recently, it has been suggested that individual differences in vulnerability to acute sleep disturbance may be a marker for an increased risk of developing chronic primary insomnia.[13] Assessing the significance of individual variation in the vulnerability to sleep disruption requires both a robust definition of the at-risk population, eg, through the evaluation of the consistent response to multiple short-term sleep-related challenges,[14,15] and longitudinal data on the evolution of chronic insomnia within that population.[2,8,16] Work along these lines is certainly incomplete, but studies that have investigated the sleep-disturbing effects of stressful stimuli have provided a basis for understanding some of the fundamental principles that must guide future investigations.[14,17-22]

Multiple stimuli, including environmental,[13,17-19,21-24] circadian,[15,25] pharmacologic,[14,26] infectious illness,[20] and stress-related challenges[27] produce sleep disturbance in some, but not all, individuals. This variability is consistent with variation in an underlying general vulnerability to transient sleep disruption,[13] but these studies also demonstrate that a variety of influences may modulate susceptibility to sleep disruption. For example in 1 study, healthy moderately sleepy and alert individuals, as defined by baseline Multiple Sleep Latency Test (MSLT), were phase advanced by 4 hours, and the effects of this "circadian" challenge on

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nocturnal sleep were determined.[15] Results indicated that individuals in the sleepy group showed less sleep disruption in response to the phase-advance challenge when compared to MSLT-defined "alert" individuals. The ability to obtain sleep despite a disruptive challenge likely reflected the higher sleep drive secondary to sleep deprivation induced by the acute phase advance.

Similar to experimentally induced sleep deprivation, general basal sleepiness from a variety of causes has been shown to attenuate the response to sleep-related challenges. For example, both individuals with high MSLT-defined basal sleepiness and those with an experimentally imposed sleep debt have been shown to have less nocturnal sleep disturbance in response to auditory stimuli than do alert individuals.[28] Therefore, if vulnerability to sleep disturbance is viewed along a continuum from low to high, evidence suggests that sleep debt may account for the variability associated with a *reduced* vulnerability to sleep disturbance. As a result, individuals with high basal sleep efficiencies that usually accompany daytime sleepiness are likely to be *protected* from otherwise sleep-disrupting stimuli. Thus, sleep deprivation must be controlled for in studies attempting to assess the existence of an intrinsic vulnerability to sleep disturbance.

There are also some data addressing the opposite end of the continuum of vulnerability to sleep disruption. Thus, given an equivalent sleep drive, are there individuals with *increased* vulnerability to sleep disruption and which factor or factors mediate such *increased* susceptibility? In one recent study, participants were given two types of sleep-disrupting "challenges" (first-night effect and circadian phase advance) to determine the consistency of individual responses.[13] The results showed a robust correlation between responses to two of the challenge paradigms across the entire sample. In addition, when subjects were grouped according to the top and bottom 25% of sleep efficiency on the initial screening night, individuals with the highest sleep efficiency continued to sleep well during a 3-hour circadian phase advance challenge, whereas individuals with the worst sleep at screening had significantly poorer sleep following the circadian challenge. Although these data provide preliminary evidence that there are consistent differences in the response to multiple sleep-related challenges, the existence and individual determinants of a "general" vulnerability to sleep disturbance have not been thoroughly investigated. Other studies have shown that insomniacs take longer to return to sleep following experimentally induced auditory arousals[22] and that the latency to sleep following an arousal is associated with physiologic measures of stress.[21] This study also showed that auditory awakening threshold is related to presleep arousal as indexed by heart rate. These results suggest a possible link between stress, waking arousal level, and vulnerability to experimentally induced sleep disturbance.

In two classic studies of presleep arousal, the presleep arousal level of insomniacs at baseline was comparable to that of control participants following a period of exercise (see review by Rechtschaffen[29]). In addition, arousal level in the insomniacs remained high throughout sleep, while heart rate in the controls returned to baseline levels within 1 hour following termination of the exercise condition. Other studies have identified heightened arousal as evidenced by measures, including cortisol[30,31] heart rate,[32] electromyographic,[33] electroencephalographic,[34-40] and metabolic variables,[41] as indicators of a pathology of arousal in primary insomnia. In a recent study of 24-hour cortisol levels in insomniacs and controls, the presleep level of cortisol was greater in insomniacs compared with control participants.[30] Furthermore, within the insomnia patients, those with greater sleep disturbance exhibited greater levels of cortisol prior to and during sleep, suggesting an abnormality of arousal in insomniacs specifically within the hypothalamic pituitary adrenal axis. Differences in arousal between insomniacs and controls have also been demonstrated at the cognitive level,[42,43] as individuals with insomnia more readily perceive themselves as awake while they are physiologically asleep in comparison to noninsomniac controls.[43,44] Together, these results implicate an intrinsic difference in cognitive and physiologic arousal between the sleep of chronic insomniacs and controls.

The present study is a step toward demonstrating a predisposition or vulnerability to sleep disturbance and its potential association with hyperarousal, while concurrently attempting to control for factors that have previously been shown to influence individual vulnerability to sleep disturbance. Specifically, the study had several objectives. First, because studies have identified stressful life events and their appraisal as major precipitating factors for individuals with insomnia,[45,46] we set out to test for the existence of a specific construct reflecting vulnerability to stress-related sleep disturbance. This included using self-report data and factor analytic techniques to develop a psychometrically validated scale aimed at measuring individual vulnerability to sleep disruption following stress exposure. Following the development of this scale, the degree to which this self-reported vulnerability was related to polysomnographically measured sleep disturbance during a first night in the laboratory was assessed. In addition, the relationship between vulnerability to sleep disturbance and physiologic arousal was determined using MSLT and heart rate as indicators of arousal. The following hypotheses were tested (1) subjects scoring high on a measure of vulnerability to sleep disturbance will show increased sleep disturbance on a first night in the laboratory and (2) individuals with high scores on this measure will exhibit hyperarousal as indexed by elevated MSLT scores and increased heart rates in comparison to low-scoring individuals.

METHOD

Participants

Individuals participating in the present study were drawn from the general population of metropolitan Detroit in conjunction with a larger ongoing epidemiologic study investigating the prevalence of daytime sleepiness in the population. A consecutive series of 116 individuals (all participants over a 10-month period) involved in the larger protocol completed the present study. Participants were drawn from the general population of tricounty metropolitan Detroit using random digit dialing techniques. In order to maintain an unbiased sample, only individuals with significant sleep-disordered breathing (respiratory disturbance index > 10; n = 7) were excluded from analyses. No individuals had a periodic limb movement arousal index greater than 5. The data for 5 individuals were excluded from analyses due to missing nocturnal polysomnogram (PSG) measures. The final sample (n = 104) included 48 men (46%) and 56 women (54%) with a mean age of 40.4 ± 12.9 years (range = 18-65 years). All procedures were approved by the institutional review board, and informed consent was obtained from all participants. Individuals were paid for study participation.

Procedures

As part of the larger study on the epidemiology of daytime sleepiness, participants completed a brief (approximately 20-minute) telephone interview prior to coming into the laboratory. The recruitment rate for interview participation was 70%. The interview consisted of questions related to sleep and health habits, along with general information regarding medical and psychiatric history. In accordance with the larger study protocol, 63.5% of the individuals in the present study were randomly selected (63/104), and the remaining 36.5% made up an enrichment sample of subjectively sleepy individuals (Daytime Sleepiness Scale [DSS][47] scores > 10). The enrichment procedure was used in the larger study to increase the number of individuals with objectively measured daytime sleepiness to provide adequate power to compare pathologically sleepy, moderately sleepy, and alert groups on a number of variables. This enrichment procedure did not bias the overall laboratory sample because there was no correlation between subjective sleepiness (based on the DSS) and the Ford Insomnia Response to Stress Test (FIRST) scale ($r = .06$, $P = .51$). Habitual daily total sleep time was assessed during the 2 weeks immediately prior to study participation using a standard sleep diary.

Ford Insomnia Response to Stress Test

Participants completed a 27-item questionnaire (Likert-scale format) regarding sleep disturbance in response to commonly experienced stressful situations. To ensure face validity, the initial item pool was determined by soliciting 10 potential questions from each of 4 experts in the field of insomnia research. The final item pool (total items = 27) was determined by consensus agreement regarding each of the questions elicited. There were 4 response options available, and each of the questions was scored or coded in the following manner *not likely* = 1, *somewhat likely* = 2, *moderately likely* = 3, and *very likely* = 4. To ensure consistency in the measure, factor analytic techniques were used to identify specific items that were representative of the construct of "stress-related" vulnerability to sleep disturbance. Reliability of the final scale (after removal of items with low factor loadings, low reliability, or both) was determined using Cronbach's coefficient α. Test-retest reliability was determined in a subsample of individuals (n = 10) who were brought into the laboratory on 2 separate occasions separated by 2 weeks and were administered the FIRST scale on each visit.

Polysomnographic Procedures

Participants reported to the laboratory 2 hours prior to their usual bedtime, as calculated from the 2-week sleep diary obtained immediately prior to their overnight PSG. An 8.5-hour PSG was scheduled with the midpoint of the 8.5-hour time in bed set to the midpoint of each participant's averaged time in bed across the 2-week diary. The PSG recordings included electroencephalograms (C3, C4, O1, O2 referenced to contralateral ear electrodes), 2 electrooculograms (bilateral horizontal), submental electromyogram, and electrocardiogram (V5 lead) and were scored in 30-second epochs according to standard procedures.[48] In addition, leg movements were monitored using a bilateral tibialis electromyogram, and respiration was monitored using a nasal/oral thermistor. All recordings were made using Grass Heritage or Aurora digital polygraphs (Grass-Telefactor, Astromed, Inc, West Warwick, RI).

Arousal Measures

For the purposes of the present paper, hyperarousal is a construct of increased arousal mediated by the hypothalamic pituitary adrenal axis or the sympathetic nervous system. While arousal can be measured in a variety of ways, including the assessment of catecholamine levels, heart-rate variability, and other physiologic measures, in the present study we will operationalize the assessment of hyperarousal as increased heart rate, elevated MSLT scores, or both. Several previous studies provide support the use of the MSLT as a measure of arousal,[26] because it has been demonstrated that increased MSLT scores are associated with an increase in metabolic rate following caffeine administration despite caffeine-induced sleep deprivation. Also, in contrast to healthy volunteers, insomnia patients appear to have an inverse relationship between sleep loss and MSLT scores.[32] Thus, to the extent that the relationship between duration of sleep and sleepiness is overridden in these patients, we believe the MSLT is reflecting a measure of hyperarousal.

During the day following nocturnal PSG, participants were studied using a 5-trial MSLT. The timing of the MSLT was determined according to standard criteria based on the rise time of each participant (ie, 1.5 to 3 hours after awakening, at 2-hour intervals). In accordance with standard procedures, sleep latency was scored as the time in minutes from the start of the MSLT to the first epoch of any stage of sleep. Heart rate was also monitored throughout the MSLT. The mean heart rate during the first 30 seconds of each MSLT trial (always during wake) was calculated and used as an additional measure of physiologic arousal. Insomnia symptoms were assessed using a previously validated measure, the Global Sleep Assessment Questionnaire (GSAQ).[49] As part of the larger study, various psychomotor performance measures were administered during the day; however, results from this 1.5-hour performance assessment battery will not be presented in this paper.

Analyses

Following the psychometric validation of the FIRST (see scale development description above), individuals scoring high or low (median-split) were compared with regard to nocturnal PSG sleep parameters, MSLT scores, heart rate, and self-reported insomnia symptoms using analyses of covariance (ANCOVA). Age and sex were used as covariates due to group differences associated with these demographic variables. Additional analyses excluding patients reporting insomnia or exhibiting evidence of excessive daytime sleepiness on the MSLT were conducted. Pearson product-moment correlation coefficients between FIRST scores and PSG and MSLT measures were also determined to assess the strength of these associations. Where deviations from normality were present, data were transformed as appropriate to reduce type I and II error rates.

RESULTS

Based on the Scree plot, 1 factor could be reliably extracted from the total 27-question pool of FIRST items. This factor accounted for 25.7% of the total variance among all items. We utilized .4 as an item-inclusion criterion because the standard and less conservative 0.3 item-inclusion criterion was not thought to be rigorous enough given our subject pool (n = 104) and the number of questions asked. Factor loadings for questions not included in the final scale were all below .37. Based on the factor loadings, 9 items loaded above .4 on the factor. A review of these 9 questions revealed that this factor comprised a measure consistent with stress-induced sleep disturbance (9-item FIRST scale). Each of the additional factors accounted for less than 8% of the remaining variance and thus was excluded from further analyses (see excluded items and their respective factor loadings in the appendix). Once the items with acceptable factor loadings were determined, reliability of the resulting scale was examined. Cronbach's α for the final 9-item scale was .83, indicating a high level of internal consistency. Test-retest reliability was assessed by administering the FIRST scale on 2 separate occasions to a subset of the sample (n = 10). There was a 2-week interval between test administrations and the test-retest reliability coefficient = .92. Each of the 9 FIRST items, along with response choices and scoring, are listed in Table 1. The mean FIRST score was 19.9 ± 5.7 (range of 9-36). Scores were normally distributed, with the 80th percentile equal to 25, the 90th equal to 28, and the 95th equal to 29.

Table 1—Ford Insomnia Response to Stress Test

When you experience the following situations, how likely is it for you to have difficulty sleeping? Circle an answer even if you have not experienced these situations recently.

Before an important meeting the next day	Not likely	Somewhat likely	Moderately likely	Very Likely
After a stressful experience during the day	Not likely	Somewhat likely	Moderately likely	Very Likely
After a stressful experience in the evening	Not likely	Somewhat likely	Moderately likely	Very Likely
After getting bad news during the day	Not likely	Somewhat likely	Moderately likely	Very Likely
After watching a frightening movie or TV show	Not likely	Somewhat likely	Moderately likely	Very Likely
After having a bad day at work	Not likely	Somewhat likely	Moderately likely	Very Likely
After an argument	Not likely	Somewhat likely	Moderately likely	Very Likely
Before having to speak in public	Not likely	Somewhat likely	Moderately likely	Very Likely
Before going on vacation the next day	Not likely	Somewhat likely	Moderately likely	Very Likely
Scoring:	1	2	3	4

Factor Loadings: Question #1 = .58, #2 = .40, #3 = .45, #4 = .73, #5 = .48, #6 = .68, #7 = .76, #8 = .42, #9 = .51.

Polysomnography Results

After total scores on the FIRST were calculated, the entire sample was divided into individuals with low or high scores based on a median split of the data (median FIRST score = 20). Demographic and sleep data for each group are presented in Table 2. Individuals with high FIRST scores were more likely to be female and older. However, there were no differences in habitual total sleep time as assessed by sleep diary (P = .87). Because of a potential effect of age and sex on group comparisons, both variables were used as covariates in ANCOVA analyses. Individuals with high scores on the FIRST had significantly lower sleep efficiency on a first laboratory night ($F_{1,100}$ = 5.74; P =.02) as well as a significantly increased latency to stage 1 sleep ($F_{1,100}$ = 6.22; P =.01) and latency to persistent sleep ($F_{1,100}$ = 5.66; P =.02) (Figure 1). Correlations between FIRST scores and nocturnal sleep parameters were significant for sleep efficiency r = -.33; stage 1 latency r = .35, and latency to persistent sleep r = .34 (P = .001 for all).

Arousal Measures

Individuals with high FIRST scores had significantly elevated latency on the MSLT, as compared to individuals with low FIRST scores ($F_{1,93}$ = 3.74; P = .056). Although the mean MSLT of the primary sample was 11.86 ± 4.63 minutes, 6 subjects had an MSLT reflective of excessive daytime sleepiness (ie, MSLT < 5). Because we were attempting to identify a construct related to inherent vulnerability, it was important to determine that the results were not merely reflecting *invulnerability* to stress-induced sleep disruption due to excessive daytime sleepiness in these individuals. Thus, an additional analysis was conducted to compare individuals with high and low scores on the FIRST excluding all individuals with excessive daytime sleepiness (MSLT ≤ 5 minutes; n = 6; 3 in each group). Using this exclusionary criterion, mean differences between the 2 groups remained significant, with the low FIRST group having a mean sleep latency on the MSLT of 11.40 ± 3.96 minutes and the high FIRST group having a mean sleep latency of 13.52 ± 4.20 minutes; t(89) = -2.49, P = .02. The correlation between FIRST scores and MSLT results was significant (r = .24, P = .02). Heart rate was not significantly different between the groups (P > .05; Table1).

Individuals Without Any History of Insomnia

In order to make certain that current or past insomnia did not account for the relationship between FIRST scores and nocturnal PSG parameters and MSLT, analyses were performed excluding those participants with current or past insomnia. Using the GSAQ, current insomnia (difficulty falling asleep or staying asleep or nonrefreshing sleep during the past month, along with daytime sequelae) was reported in 4.9% of the sample. In individuals with low FIRST scores, 1.9% reported insomnia, whereas 8% of individuals with high FIRST scores reported insomnia. To assess the possible contribution of asymmetry in insomnia prevalence to the observed group differences, additional analyses were performed after the exclusion of all individuals reporting any current insomnia on

Table 2—Demographic and sleep* data of individuals with high and low scores on the Ford Insomnia Response to Stress Test

Sleep and Demographic Measures	Low Group (n = 54) Mean FIRST score = 15.4	High Group (n = 50) Mean FIRST score = 24.8
Age, y	36.1 ± 11.9	45.1 ± 12.3†
Women, %	41	68‡
Habitual sleep data from a 2-week sleep diary		
Time in Bed, h	7.78 ± .94	7.96 ± .97
TST, h	7.2 ± .91	7.3 ± .93
Sleep efficiency, h	93.6 ± .94	90.6 ± .94
Sleep latency, min	19.3 ± 21.2	22.8 ± 20.0
Awakenings, no.	0.6 ± .62	1.3 ± .64§
Polysomnographic data during first night in the laboratory		
TST, h	7.57 ± .97	6.82 ± 1.17§
Sleep latency, min	9.4 ± 11.4	22.5 ± 25.6§
Stage 1, %	8.8 ± 7.3	9.9 ± 6.6
Stage 2, %	57.7 ± 7.9	54.4 ± 11.8
Stage 3-4, %	12.9 ± 8.1	14.9 ± 9.7
REM, %	20.7 ± 6.1	20.7 ± 7.0
Daytime heart rate, bpm	69.4 ± 10.4	70.7 ± 9.5

*Data are presented as mean ± SD. †P < .05 (t-test); ‡P < .05 (X^2); §P < .05 (analysis of covariance with age and sex as covariates). FIRST refers to Ford Insomnia Response to Stress Test; TST, total sleep time; REM, rapid eye movement; bpm, beats per minute.

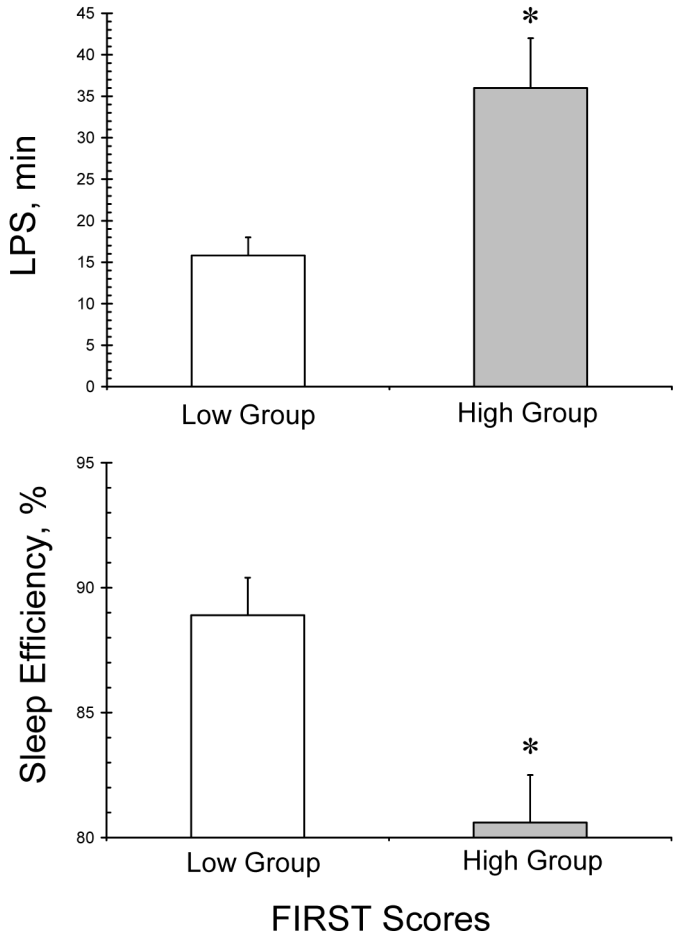

Figure 1—Mean ± SEM sleep efficiency and latency to persistent sleep (LPS) in groups with low and high scores on the Ford Insomnia Response to Stress Test (FIRST) (*P < .05 using analysis of covariance with age and sex as covariates).

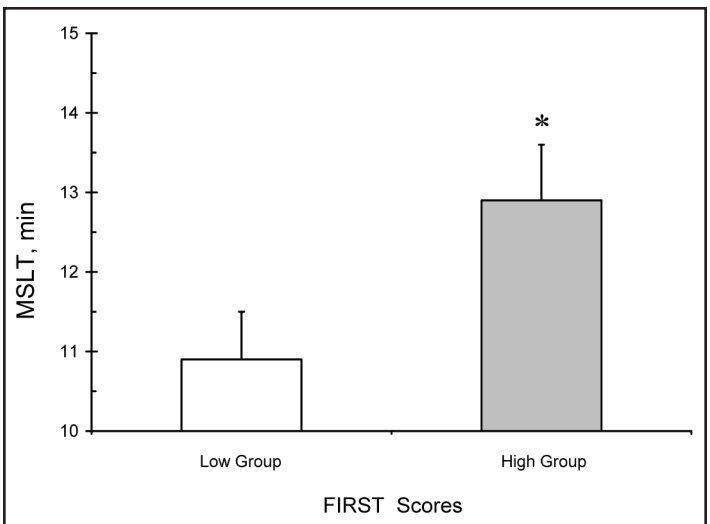

Figure 2—Mean ± SEM sleep latency on the Multiple Sleep Latency Test (MSLT) in groups with low and high scores on the Ford Insomnia Response to Stress Test (FIRST) (*P = .056 versus group with low scores on the FIRST using analysis of covariance with age and sex as covariates).

the GSAQ (n = 5; GSAQ not available in 1 subject). After excluding preexisting insomnia, the differences in sleep efficiency, latency to sleep, and MSLT remained significant (see Table 3). Correlations between FIRST scores and nocturnal PSG and MSLT variables also remained significant after the exclusion of individuals with current insomnia (r = .29 to .36, P < .01 for all). When all individuals with any lifetime history of insomnia symptoms were excluded (n = 60), results remained significant for the nocturnal polysomnographic parameters but not the MSLT results.

DISCUSSION

The present findings are the first to demonstrate that individuals who score high on a measure of stress-related sleep disturbance have greater sleep disruption on the first night in the laboratory. These differences in sleep as a function of FIRST scores support the hypothesis that there are individual differences in vulnerability to transient insomnia. These results are consistent with previous studies of transient insomnia[13,27,50] and show that particular individuals may have a vulnerability to sleep disturbance induced by stress. Moreover, the results demonstrate that this vulnerability can be reliably assessed, is associated with physiological hyperarousal, and is present independent of exogenous influences such as excessive daytime sleepiness.

It cannot be definitively concluded that the PSG results are reflective of a first-night effect because only 1 laboratory night was assessed and attempts to demonstrate a first-night effect have not always been confirmed.[51] However, the sleep efficiency of the present sample is similar to previous studies that found a first-night effect,[17,51-57] and sleep efficiency in the present study was considerably lower than that found following adaptation to the sleep laboratory.[58] One alternative explanation is that the differences found in the present study reflect basal sleep disturbance between the 2 groups. However, the study findings were similar when individuals who reported insomnia were excluded from the analyses. In addition, on sleep diaries completed prior to the laboratory night, reported habitual total sleep time was not different between the groups, suggesting that a first-night effect rather than basal sleep disturbance is likely to account for the differences observed. Future studies would benefit from additional PSG nights in order to identify the individual magnitude of a first-night effect in relation to FIRST scores. Future studies are needed to determine whether individuals with high FIRST scores, especially those without insomnia, also show sleep disturbance in response to other sleep-disrupting challenges such as acute stress, drug administration, and shifts in circadian phase.

It is interesting to note that, as in the present study, most studies of insomnia have not found a robust correlation between insomnia or its severity and subsequent PSG-measured sleep in the laboratory. However, scores on the FIRST were positively associated with poor PSG-measured sleep in both the full sample and in individuals without insomnia in the present study. Together, these findings suggest that variability in objectively measured sleep may be accounted for by scores on the FIRST. The present study was aimed at identifying the individual factors that may predispose individuals to experiencing transient insomnia. However, recent findings linking chronic primary insomnia and hyperarousal evidenced by cognitive,[42,43] endocrine,[30,31] and neurophysiologic[34,35,37,38] variables, along with the relationship between daytime hyperarousal and susceptibility to acute sleep disturbance in the present study, suggests that hyperarousal may represent a marker of vulnerability to transient as well as chronic sleep disturbance.

Although heart rate was not significantly related to FIRST scores in the present study, average heart rate is not a reliable measure of autonomic arousal. A more selective measure such as high-or low-frequency heart-rate variability[59] would provide a better noninvasive measure of arousal. Future studies may benefit by employing selective measures of autonomic arousal such as measuring catecholamine levels, pupillary light responses, or impedance cardiography to evaluate individuals who are susceptible to experiencing transient insomnia. Subjective measures of hyperarousal and their association with the current scale should also be assessed to determine the extent to which transient sleep disruption leads to complaints of insomnia. Equally important, researchers will need to investigate the sleep of individuals who report having an episode of transit insomnia to determine whether there is objective evidence of sleep disturbance. These types of studies are critical for establishing the temporal links between vulnerability to sleep disruption and episodes of transient or chronic insomnia. Contrary to what one might expect given the association between hyperarousal on the MSLT and high FIRST scores, subjective sleepiness as measured by the DSS was not correlated with the FIRST scale. However, similar to heart rate, the DSS is not likely to be a specific and sensitive indicator of arousal due to the multiple factors that can influence this measure. Additional studies will be needed to determine possible links between additional indicators of arousal and the FIRST scale.

Consistent with the present findings, several previous studies have shown a relationship between insomnia and personality characteristics related to stress such as worry, rumination, and being upset or angry after interpersonal conflict.[45,60-71] Specifically, Kales and Kales[72] noted the importance of stressful events on the development of chronic insomnia and stated that "stressful events… when mediated by certain predisposing emotional factors and inadequate coping mechanisms, are indeed closely related to the onset of long-term sleep difficulty." Although the specific emotional factors that may predispose individuals to insomnia have not been determined, data suggest that the personality trait of neuroticism and the internalization of stressful events may play a significant role.[61,65] Thus, longitudinal research investigating the relationship between the present scale and trait measures of neuroticism, along with their possible association with the risk for developing chronic primary insomnia, may be a valuable area for future study.

Most importantly, the results of the present paper may have significant implications as to the etiology of chronic insomnia. While an association between elevated FIRST scores and vulnerability to experiencing transient insomnia does not, by itself, directly address the evolution to chronic insomnia, other factors suggest that these findings may be relevant to the development of that disorder. First, the elevated latencies on MSLT in these individuals, despite disturbed nocturnal sleep, suggest that these individuals, like those with chronic primary insomnia,[30-32,41,59] exhibit physiologic hyperarousal. Second, there are important similarities between the population scoring high on the FIRST and those at risk for developing chronic primary insomnia in age (older) and sex (more women) distributions. These findings suggest that individuals who report an elevated response to stress-induced sleep disruption may be not only vulnerable to transient insomnia, but also predisposed to developing a more chronic sleep disturbance.

Table 3—Polysomnographic and Multiple Sleep Latency Test values* for individuals without current insomnia in both high and low FIRST groups.

Dependent Measure	Low Group (n = 52)	High Group (n = 46)
Sleep efficiency, %	88.9 ± 11.4	80.6 ± 14.1†
Sleep latency, min	9.2 ± 11.6	22.6 ± 26.6†
LPS, min	15.6 ± 16.2	36.8 ± 44.1†
Stage 1, %	8.8 ± 7.5	10.1 ± 6.7
Stage 2, %	58.0 ± 7.8	53.6 ± 11.0†
Stage 3-4, %	12.7 ± 8.2	15.0 ± 9.8
REM, %	20.5 ± 6.1	21.2 ± 7.0
MSLT, min	10.8 ± 4.3	13.1 ± 4.7†
Heart rate, bpm	69.1 ± 10.4	70.2 ± 9.4

Data are presented as mean ± SD
†P < .05 (analysis of covariance with age and sex as covariates)
FIRST refers to Ford Insomnia Response to Stress Test; LPS, latency to 10 minutes of persistent sleep (ie, no intervening wake epochs); REM, rapid eye movement; MSLT, Multiple Sleep Latency Test; bpm, beats per minute.

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APPENDIX

Excluded items (Loading)
Sleeping away from home (.10)
After going to bed late (.08)
After drinking alcohol in the evening (.27)
After going to bed early (.01)
Experiencing jet lag (.17)
Sleeping in a hot bedroom (.27)
After having slept badly the night before (.05)
After having been awakened during the night (.29)
Before having to wake up early (.24)
After drinking caffeinated beverages in the evening (.17)
When having pain (.37)
After the death of a loved one (.37)
After a physically strenuous day (.07)
After having been depressed during the day (.29)
After being anxious during the day (.36)
Sleeping alone (.09)
Sleeping in a noisy environment (.25)
Anticipating having to wakeup during the night (eg, new baby, on call) (.29)

REFERENCES

1. Chevalier H, Los F, Boichut D, Bianchi M, Nutt DJ, Hajak G, Hetta J, Hoffmann G, Crowe C. Evaluation of severe insomnia in the general population: Results of a european multinational survey. Journal of Psychopharmacology. 1999;13:S21-24.
2. Janson C, Lindberg E, Gislason T, Elmasry A, Boman G. Insomnia in men-a 10-year prospective population based study. Sleep 2001;24:425-430.
3. Leger D, Guilleminault C, Bader G, vy E, Paillard M. Medical and socio-professional impact of insomnia. Sleep 2002;25:625-629.
4. Leger D, Scheuermaier K, Philip P, Paillard M, Guilleminault C. Sf-36: Evaluation of quality of life in severe and mild insomniacs compared with good sleepers. Psychosomatic Medicine. 2001;63:49-55.
5. Katz DA, McHorney CA. The relationship between insomnia and health-related quality of life in patients with chronic illness. Journal of Family Practice. 2002;51:229-235.
6. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-1484.
7. Perlis ML, Giles DE, Buysse DJ, Tu X, et al. Self-reported sleep disturbance as a prodromal symptom in recurrent depression. Journal of Affective Disorders 1997;42:209-212.
8. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: A longitudinal epidemiological study of young adults. Biol Psychiatry 1996;39:411-418.
9. Chang PP, Ford DE, Mead LA, Cooper-Patrick L, Klag MJ. Insomnia in young men and subsequent depression. The johns hopkins precursors study. Am J Epidemiol 1997;146:105-114.
10. Agargun MY, Kara H, Solmaz M. Sleep disturbances and suicidal behavior in patients with major depression. Journal of Clinical Psychiatry 1997;58:249-251.
11. Leger D. Public health and insomnia: Economic impact. Sleep. 2000;23:S69-76.
12. Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. Psychiatr Clin North Am 1987;10:541-553.
13. Bonnet M, Arand DL. Situational insomnia: In the situation or in the patient? Sleep, Abstract Supplement 2002;25:A32-A33.
14. Karacan I, Thornby JI, Anch M, Booth GH, Williams RL, Salis PJ. Dose-related sleep disturbances induced by coffee and caffeine. Clin Pharmacol Ther 1976;20:682-689.
15. Roehrs T, Salin-Pascual R, Merlotti L, Rosenthal L, Roth T. Phase advance in moderately sleepy and alert normals. Sleep 1996;19:417-422.
16. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: An epidemiologic study of 6,800 persons over three years. Sleep 1999;22 Suppl 2:S366-372.
17. Agnew HW, Jr., Webb WB, Williams RL. The first night effect: An eeg study of sleep. Psychophysiology 1966;2:263-266.
18. Browman CP, Cartwright RD. The first-night effect on sleep and dreams. Biol Psychiatry 1980;15:809-812.
19. Terzano MG, Parrino L, Fioriti G, Orofiamma B, Depoortere H. Modifications of sleep structure induced by increasing levels of acoustic perturbation in normal subjects. Electroencephalogr Clin Neurophysiol 1990;76:29-38.
20. Drake CL, Roehrs TA, Royer H, Koshorek G, Turner RB, Roth T. Effects of an experimentally induced rhinovirus cold on sleep, performance, and daytime alertness. Physiol Behav 2000;71:75-81.
21. Haynes SN, Fitzgerald SG, Shute G, O'Meary M. Responses of psychophysiologic and subjective insomniacs to auditory stimuli during sleep: A replication and extension. J Abnorm Psychol 1985;94:338-345.
22. Johnson LC, Church MW, Seales DM, Rossiter VS. Auditory arousal thresholds of good sleepers and poor sleepers with and without flurazepam. Sleep 1979;1:259-270.
23. Roth T, Roehrs T, Vogel G. Zolpidem in the treatment of transient insomnia: A double-blind, randomized comparison with placebo. Sleep 1995;18:246-251.
24. Roehrs T, Vogel G, Sterling W, Roth T. Dose effects of temazepam in transient insomnia. Arzneimittelforschung 1990;40:859-862.
25. Erman MK, Erwin CW, Gengo FM, Jamieson AO, Lemmi H, Mahowald MW, Regestein QR, Roth T, Roth-Schechter B, Scharf MB, Vogel GW, Walsh JK, Ware JC. Comparative efficacy of zolpidem and temazepam in transient insomnia. Hum Psychopharmacol 2001;16:169-176.
26. Bonnet MH, Arand DL. Caffeine use as a model of acute and chronic insomnia. Sleep 1992;15:526-536.
27. Craske MG, Lang AJ, Rowe M, DeCola JP, Simmons J, Mann C, Yan-Go F, Bystritsky A. Presleep attributions about arousal during sleep: Nocturnal panic. J Abnorm Psychol 2002;111:53-62.
28. Rosenthal L, Bishop C, Helmus T, Krstevska S, Roehrs T, Roth T. Auditory awakening thresholds in sleepy and alert individuals. Sleep 1996;19:290-295.
29. Rechtschaffen A. Polygraphic aspects of insomnia. Paper presented at: The Abnormalities of Sleep in Man; 1968, 1968; Bologna.
30. Vgontzas AN, Bixler EO, Lin HM, Prolo P, Mastorakos G, Vela-Bueno A, Kales A, Chrousos GP. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: Clinical implications. J Clin Endocrinol Metab 2001;86:3787-3794.
31. Vgontzas AN, Tsigos C, Bixler EO, Stratakis CA, Zachman K, Kales A, Vela-Bueno A, Chrousos GP. Chronic insomnia and activity of the stress system: A preliminary study. Journal of Psychosomatic Research 1998;45:21-31.
32. 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.
33. Haynes SN, Follingstad DR, McGowan WT. Insomnia: Sleep patterns and anxiety level. J Psychosom Res 1974;18:69-74.
34. Freedman RR. Eeg power spectra in sleep-onset insomnia. Electroencephalogr Clin Neurophysiol 1986;63:408-413.
35. Lamarche CH, Ogilvie RD. Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and normal sleepers. Sleep 1997;20:724-733.
36. Merica H, Gaillard JM. The eeg of the sleep onset period in insomnia: A discriminant analysis. Physiol Behav 1992;52:199-204.
37. Merica H, Blois R, Gaillard JM. Spectral characteristics of sleep eeg in chronic insomnia. Eur J Neurosci 1998;10:1826-1834.
38. Perlis ML, Smith MT, Andrews PJ, Orff H, Giles DE. Beta/gamma eeg activity in patients with primary and secondary insomnia and good sleeper controls. Sleep 2001;24:110-117.
39. Perlis ML, Kehr EL, Smith MT, Andrews PJ, Orff H, Giles DE. Temporal and stagewise distribution of high frequency eeg activity in patients with primary and secondary insomnia and in good sleeper controls. J Sleep Res 2001;10:93-104.
40. Nofzinger E, Nowell P, Buysee D. Towards a neurobiology of sleep disturbance in primary insomnia and depression: A comparison of subjective, visually scored period amplitude, and power spectral density sleep measures. Sleep 1999;22:S99-S99.
41. Bonnet MH, Arand DL. 24-hour metabolic rate in insomniacs and matched normal sleepers. Sleep 1995;18:581-588.
42. Wicklow A, Espie CA. Intrusive thoughts and their relationship to actigraphic measurement of sleep: Towards a cognitive model of insomnia. Behav Res Ther 2000;38:679-693.
43. Perlis ML, Giles DE, Mendelson WB, Bootzin RR, Wyatt JK. Psychophysiological insomnia: The behavioural model and a neurocognitive perspective. J Sleep Res 1997;6:179-188.
44. Knab B, Engel RR. Perception of waking and sleeping: Possible implications for the evaluation of insomnia. Sleep 1988;11:265-272.
45. Healey ES, Kales A, Monroe LJ, Bixler EO, Chamberlin K, Soldatos CR. Onset of insomnia: Role of life-stress events. Psychosom Med 1981;43:439-451.
46. Morin CM, Rodrigue S, Ivers H. Role of stress, arousal, and coping skills in primary insomnia. Psychosom Med 2003;65:259-267.
47. Johnson EO, Breslau N, Roth T, Roehrs T, Rosenthal L. Psychometric evaluation of daytime sleepiness and nocturnal sleep onset scales in a representative community sample. Biol Psychiatry 1999;45:764-770.
48. Rechtschaffen A, Kales A. A manual of standardized, techniques and scoring system for sleep stages of human sleep. Los Angeles: Brain Information Service/Brain Research Institute, University of California at Los Angeles,. 1968.
49. Roth T, Zammit G, Kushida C, Doghramji K, Mathias SD, Wong JM, Buysse DJ. A new questionnaire to detect sleep disorders. Sleep Medicine 2002;3:99-108.
50. Vein AM, Sudakov KV, Levin YI, Yumatov EA, Strygin KN, Kovrov GV. Stages of sleep after psychoemotional tension: The individual character of changes. Neurosci Behav Physiol 2002;32:513-518.
51. Kader GA, Griffin PT. Reevaluation of the phenomena of the first night effect. Sleep 1983;6:67-71.
52. Le Bon O, Staner L, Hoffmann G, Dramaix M, San Sebastian I, Murphy JR, Kentos M, Pelc I, Linkowski P. The first-night effect may last more than one night. J Psychiatr Res 2001;35:165-172.
53. Lorenzo JL, Barbanoj MJ. Variability of sleep parameters across multiple laboratory sessions in healthy young subjects: The "very first night effect". Psychophysiology 2002;39:409-413.
54. Riedel BW, Winfield CF, Lichstein KL. First night effect and reverse first night effect in older adults with primary insomnia: Does anxiety play a role? 2001;2:125-133.
55. Toussaint M, Luthringer R, Schaltenbrand N, Carelli G, Lainey E, Jacqmin A, Muzet A, Macher JP. First-night effect in normal subjects and psychiatric inpatients. Sleep 1995;18:463-469.
56. Wauquier A, van Sweden B, Kerkhof GA, Kamphuisen HA. Ambulatory first night sleep effect recording in the elderly. Behav Brain Res 1991;42:7-11.

57. Webb WB, Campbell SS. The first night effect revisited with age as a variable. Waking Sleeping 1979;3:319-324.
58. Stepanski E, Roehrs T, Saab P, Zorick F, Roth T. Readaption to the sleep laboratory in long-term sleep studies. Bulletin of the Psychonomic Society 1981;17:224-226.
59. Bonnet MH, Arand DL. Heart rate variability in insomniacs and matched normal sleepers. Psychosom Med 1998;60:610-615.
60. Morgan K, Healey DW, Healey PJ. Factors influencing persistent subjective insomnia in old age: A follow-up study of good and poor sleepers aged 65 to 74. Age Ageing 1989;18:117-122.
61. Scofield H, Jefferson C, Roehrs T, Burduvali E, Roth T. Neuroticism predicts lifetime prevalence of insomnia. Sleep 2002;Abstract Supplement:A96.
62. Bertelson AD, Monroe LJ. Personality patterns of adolescent poor and good sleepers. J Abnorm Child Psychol 1979;7:191-197.
63. Kales A, Caldwell AB, Preston TA, Healey S, Kales JD. Personality patterns in insomnia. Theoretical implications. Arch Gen Psychiatry 1976;33:1128-1124.
64. Soldatos CR, Kales A. Sleep disorders: Research in psychopathology and its practical implications. Acta Psychiatr Scand 1982;65:381-387.
65. Kales A, Caldwell AB, Soldatos CR, Bixler EO, Kales JD. Biopsychobehavioral correlates of insomnia. Ii. Pattern specificity and consistency with the minnesota multiphasic personality inventory. Psychosom Med 1983;45:341-356.
66. Kales JD, Kales A, Bixler EO, Soldatos CR, Cadieux RJ, Kashurba GJ, Vela-Bueno A. Biopsychobehavioral correlates of insomnia, v: Clinical characteristics and behavioral correlates. Am J Psychiatry 1984;141:1371-1376.
67. Kales A, Bixler EO, Vela-Bueno A, Cadieux RJ, Soldatos CR, Kales JD. Biopsychobehavioral correlates of insomnia, iii: Polygraphic findings of sleep difficulty and their relationship to psychopathology. Int J Neurosci 1984;23:43-55.
68. Tan TL, Kales JD, Kales A, Soldatos CR, Bixler EO. Biopsychobehavioral correlates of insomnia. Iv: Diagnosis based on dsm-iii. Am J Psychiatry 1984;141:357-362.
69. Coursey RD, Frankel BL. Novelty-seeking, fantasy, and sensitization in chronic insomniacs. Percept Mot Skills 1977;44:795-798.
70. Coursey RD. Personality measures and evoked responses in chronic insomniacs. J Abnorm Psychol 1975;84:239-249.
71. Salin-Pascual RJ, Roehrs TA, Merlotti LA, Zorick F, Roth T. Long-term study of the sleep of insomnia patients with sleep state misperception and other insomnia patients. Am J Psychiatry 1992;149:904-908.
72. Kales A, Kales JD. Psychiatric factors in insomnia. In: Kales A, Kales JD, eds. Evaluation and treatment of insomnia. New York: Oxford Univ. Press; 1984:111.