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Does Physiological Hyperarousal Enhance Error Rates among Insomnia Sufferers?

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Objective: To examine the association between physiological hyperarousal and response accuracy on reaction time tasks among individuals with insomnia.

Design and Setting: This study was conducted at affiliated Veterans Administration (VA) and academic medical centers using a matched-group, cross-sectional research design.

Participants: Eighty-nine individuals (48 women) with primary insomnia, PI (M_{Age} = 49.8 ± 17.2 y) and 95 individuals (48 women) who were well-screened normal sleepers, NS (M_{Age} = 46.9 ± 17.0 y).

Methods and Measures: Participants underwent 3 nights of polysomnography followed by daytime testing with a four-trial Multiple Sleep Latency Test (MSLT). Before each MSLT nap, they rated their sleepiness and completed computer-administered reaction time tasks. The mean number of correct and error responses made by each participant across testing trials served as dependent measures. The PI and NS groups were each subdivided into alert (e.g., MSLT mean onset latency > 8 min) and sleepy (e.g., MSLT mean onset latency ≤ 8 min) subgroups to allow for testing the main and interaction effects of participant type and level of alertness.

Results: Alert participants had longer MSLT latencies than sleepy participants (12.7 versus 5.4 min), yet both alert and sleepy individuals with PI reported greater sleepiness than NS. Alert participants also showed lower sleep efficiencies (83.5% versus 86.2%, P = 0.03), suggesting 24-h physiological hyperarousal particularly in the PI group. Individuals with PI had fewer correct responses on performance testing than did NS, whereas a significant group × alertness interaction (P = 0.0013) showed greater error rates among alert individuals with PI (mean = 4.5 ± 3.6 errors per trial) than among alert NS (mean = 2.6 ± 1.9 errors per trial).

Conclusions: Physiological hyperarousal in insomnia may lead to more apparent daytime alertness yet dispose individuals with insomnia to higher error rates on tasks requiring their attention.

Keywords: MSLT, performance errors, physiological hyperarousal, primary insomnia

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INTRODUCTION

Whereas the pathophysiology of insomnia remains poorly understood, a substantial body of research implicates a dysfunction in the modulation of arousal. Bonnet and Arand,[1] for example, showed that individuals with primary insomnia (PI) manifest a higher metabolic rate across the 24-h day than do matched noncomplaining normal sleepers (NS). Subsequently, these same researchers found that, relative to their normal sleeping counterparts, those with PI showed reduced heart rate variability from daytime to nighttime, suggesting less deactivation during the sleep period.[2] Complementing such findings, Vgontzas et al.[3] showed that individuals with PI have higher levels of serum cortisol across the 24-h day and particularly during presleep and sleep periods than do normal control individuals. In addition, studies using both spectral analysis of the sleep electroencephalogram (EEG)[4,5] as well as positron emission tomography (PET) scans taken shortly after nocturnal awakenings[6] suggest a relatively blunted central nervous system deactivation during sleep among individuals with insomnia compared with those without sleep difficulties. These findings imply that the sleep difficulties of those with PI are accompanied by and possibly perpetuated by unrelenting physiological hyperarousal.

Along with its sleep-disruptive effects, the pathological hyperarousal in PI also has notable manifestations in various aspects of daytime functioning. Several studies[7-9] have documented that individuals with PI appear substantially more alert on daytime testing with the Multiple Sleep Latency Test (MSLT) than do age- and sex-matched NS. Hence, any objective sleepiness that might result from relative nocturnal sleep deficits in individuals with PI appears overridden by their chronic hyperaroused state. Less clear is whether their physiological hyperarousal is accompanied by alterations in neurocognitive functioning. A number of investigations have found no significant differences between individuals with PI and NS on a range of cognitive performance tests.[10] A recent example of these studies is the one by Orff et al.,[11] which showed that individuals with PI had complaints about daytime dysfunction yet showed no greater deficits on a battery of cognitive tests than did matched NS. These authors interpret their findings as suggesting that individuals with PI have either an attention bias or realistic appraisal so that enhanced effort is needed to maintain normal cognitive performance. Such findings also have been interpreted as implying that physiological hyperarousal may help those with PI offset any cognitive effects they might otherwise incur from their ongoing sleep disturbances. However, it has been noted that many of these studies used small samples and assessment procedures insensitive to the sorts of daytime deficits of which PI patients complain.[9] Moreover, with a large sample and sensitive reaction time tests we did demonstrate

A commentary on this article appears in this issue on page 1125.

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that individuals with PI do show slower and more variable reaction times than do NS, particularly in response to complex tasks.[9] More recently, Fernandez-Mendoza et al.[12] showed that a subgroup of individuals with PI who manifest physiological hyperarousal as reflected by an objective short sleep duration (i.e., < 6 h per night by polysomnography [PSG]) showed significantly poorer performances on a neurocognitive test battery than did NS with either normal or short sleep durations. Given these latter findings, it is unclear that physiological hyperarousal of individuals with PI offsets deficits they may have in all cognitive domains.

However, PI is a fairly global diagnosis that encompasses a rather heterogeneous group of those with insomnia complaints. Given this consideration it seems possible, if not probable, that physiological hyperarousal may not be a trait common to all who share this diagnosis. In this regard Vgontzas et al.[13] and Fernandez-Mendoza et al.[14] have proposed two subtypes with insomnia complaints. One of these is characterized by the physiological hyperarousal syndrome that results in objective sleep disturbances and substantial psychiatric, medical, and neurocognitive morbidity, whereas the second is characterized by a more normal sleep pattern and lower morbidity rates. Thus, it would seem useful to discriminate those with and without this sort of physiological hyperarousal so that its effects on the daytime functioning of those with PI can be isolated and clarified.

In the current investigation we attempted to discern the effects of physiological hyperarousal on the rates of correct and error responses made by those with PI in response to reaction time tasks. To do so we used MSLT results as an assay for discriminating highly alert and sleepy groups of individuals with PI and NS. We then compared the correct and error response rates of these subgroups across a four-trial set of reaction time tasks administered over the course of a day-long testing protocol. Our primary study objective was to determine whether those individuals with insomnia with the MSLT-defined physiological hyperarousal pattern were more or less disposed to performance deficits than were either their nonaroused PI counterparts or the alert and sleepy subgroups of NS.

METHOD

Design

This study used a between-groups cross-sectional research design. Matched groups of individuals with PI and noncomplaining NS comprised the study sample. Participants of the current study were drawn from a parent study[9,15,16] conducted to compare the home and laboratory sleep patterns of adults with insomnia and NS. The original study protocol was reviewed and approved by the Institutional Review Boards of the VA Medical Center and Duke University Medical Center in Durham, NC. All participants provided written informed consent prior to enrollment. At the conclusion of their study involvement, all participants received compensation for parking expenses and completion of study procedures.

Participants

Participants included three separate cohorts recruited via posted announcements at a VA and affiliated university medical center, flyers posted in public libraries, letters mailed to persons in Duke University's Center for the Study of Aging and Human Development Subject Pool, and face-to-face solicitations of patients presenting to the Duke Sleep Disorders Center. A senior cohort (age 60-79 y) was recruited between October 1992 and July 1994, a second, middle-aged (age 40-59 y) group was recruited between October 1995 and July 1997, and the final young cohort (age 20-39 y) was recruited between October 1999 and October 2001. Each cohort included age- and sex-matched individuals with PI and NS.

Study candidates first underwent a screening composed of structured psychiatric (Structured Clinical Interview for Psychiatric Disorders, SCID)[17] and sleep interviews,[18] a medical examination, thyroid (thyroid-stimulating hormone level) screening, and 1 to 2 nights of PSG to rule out occult primary sleep disorders. The individuals with insomnia met slightly modified Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR) criteria for PI. Consistent with DSM-IV-TR, our study participants with insomnia had to report difficulty initiating or maintaining sleep or nonrestorative sleep with accompanying daytime deficits.[19,20] However, to ensure the chronicity of their symptoms, they also were required to report at least a 6-month duration of insomnia symptoms rather than the 1-month minimum required by the DSM-IV-TR. The NS enrolled were adults who reported no sleep complaints and had no major medical condition based on history and physical examination and no psychiatric condition by history or on SCID screening. Those excluded had (1) a sleep-disruptive medical condition (e.g., rheumatoid arthritis); (2) a current major psychiatric (Axis I) condition on the basis of SCID[17]; (3) sedative hypnotic dependence and unwillingness/inability to abstain from these medications while in the study; (4) use of anxiolytic agents, antidepressant agents, or any other psychotropic medication; or (5) an apnea-hypopnea index (AHI) $\geq$ 15 or a periodic limb movement-related Arousal Index $\geq$ 15 during screening PSG; (6) evidence of a comorbid sleep in addition to PI on the structured sleep interview.[18]

A total of 205 volunteers enrolled, but 21 were dropped from the study because they failed to complete the study procedures relevant to this report. Therefore, the final sample included 184 participants. Eighty-nine participants met criteria for PI whereas the remaining 95 met the selection criteria for NS. Table 1 provides demographic information for the sample. The insomnia and NS groups did not differ significantly in regard to their mean ages (F [1,182] = 1.30, $P = 0.26$), sex composition (χ^2 (1) = 0.21, $P = 0.64$) or ethnic group composition (χ^2 (4) = 2.98, $P = 0.56$).

Polysomnography

As part of the parent study protocol, all participants underwent 3 consecutive nights of PSG conducted either in their homes or in our university medical center's sleep laboratory just prior to the daytime testing protocol described in the next paragraphs. The location of PSGs (laboratory versus home) was randomly determined so that approximately half of the men and women in each study sample underwent laboartory recording (44 PI, 47 NS), and the other half completed home monitoring (45 PI, 48 NS) before their daytime testing. All PSGs were conducted using eight-channel Oxford Medilog® 9000 or 9200 series (Oxford Medical, Inc., Clearwater, Fl) ambulatory cassette recorders. The monitoring montage included two EEG channels

(C_3-A_2, O_z-C_z), bilateral electrooculogram (EOG), submental electromyogram (EMG), two channels of anterior tibialis EMG (right and left leg), and a nasal-oral thermistor. All PSGs were scored using standard scoring criteria for assignment of sleep stages, identification of respiratory events (e.g., apneas, hypopneas) and identification of periodic limb movements and periodic limb movement-related arousals.[21-24] The first PSG night (home or laboratory) in the older cohort (age 60+ y) or the initial 2 PSG nights in the remainder of the sample were used to screen out those exceeding the aforementioned apnea-hypopnea or periodic limb movement arousal cutoffs for study inclusion. Although PSG typically includes additional respiratory measures (respiratory effort, oximetry) to detect breathing abnormalities, it was thought that monitoring of nasal/oral airflow along with our thorough interview screening for apnea would be sufficient to identify almost all cases with an AHI higher than the study's exclusionary cutoff. In addition to the screening data, mean values of time in bed (TIB) total sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO), and sleep efficiency (SE) were derived from the three PSGs conducted prior to daytime testing and were used in study analyses.

Table 1—Demographic characteristics of the study sample

Demographic Characteristic	Primary Insomnia Group	Normal Sleepers
Age, years, mean (SD)	49.8 (17.2)	46.9 (17.0)
Years of education, mean (SD)	15.2 (3.0)	15.9 (2.8)
Ethnicity, n		
Caucasian	67	78
African American	15	12
Other	7	5
Duration of insomnia, years, mean (SD)	10.7 (9.0)	–
Presenting problem, n		–
Onset difficulty	15	
Maintenance difficulty	27	
Both onset and maintenance difficulty	42	
Other	5	

SD, standard deviation.

Daytime Protocol

On the day immediately following their third consecutive PSG recording, participants spent 1 day in the sleep laboratory to complete testing designed to measure their daytime sleepiness and neurocognitive functioning. The assessment protocol commenced 2-3 h after participants' respective morning rising times and comprised a four-trial MSLT with each nap trial preceded by a 20-min battery of computer-administered reaction time tests and then an administration of the Stanford Sleepiness Scale.[25] Per standard MSLT procedures, the daytime testing was scheduled so each of the four performance testing and sleepiness assessment trials occurred 2 h apart. All daytime testing was conducted under the supervision of trained laboratory technologists. Immediately prior to initiating daytime testing, participants' PSG electrodes were checked and readjusted if necessary. Participants were supervised between trials to prevent unscheduled sleep episodes. PSG electrodes were worn for the entire day of laboratory testing and were not removed until after the final trial was completed. Once the fourth performance/MSLT trial was completed and electrodes were removed, the participant was allowed to leave the laboratory.

The performance battery was taken from the Neurobehavioral Evaluation System (NES)[26] and included a simple reaction time test, followed by a continuous performance test (CPT) and then a switching attention task (SAT). All three tests provided measures of participants' reaction times to stimulus items, but the latter two tests also provided tallies of correct and incorrect responses. Because response accuracy was the focus of this study, only data from those two tests were selected for analyses. The CPT consisted of a signal detection task during which a target (i.e., the letter *S*) and background stimuli (i.e., the letters A, C, E, and T) were presented in random order on the computer screen with a 1:4 target-to-background ratio throughout testing. The various letters were presented at the rate of 1 per sec with each letter remaining on the screen for 50 msec. The total test lasted approximately 5 min and included 60 presentations of the target and 240 presentations of the background stimuli. Participants were required to press a specially marked key on the computer keyboard when and only when the target letter appeared. Tallies of correct responses to the target as well as errors (i.e., responses to the nontarget letters + failures to respond to the target) were obtained for each participant for each trial.

The subsequent SAT lasted approximately 6 min and included a range of reaction time tasks. During the first section of the SAT, a square appeared on the right or left side of the computer screen and the participant was required to press a marked key on the corresponding side of the keyboard. During the second such task, an arrow pointing right or left appeared in the center of the screen, and the participant was required to make a right or left side key press in response as directed by the arrow. During each of these tasks, the stimulus remained on the screen either until a response occurred or 2,500 msec had elapsed. The former of the two tasks included six practice and 16 test presentations of the stimulus, whereas the latter included four practice and 16 test presentations of the stimulus during each testing trial. During the final, most complex portion of the SAT, an arrow (pointing right or left) appeared either on the right or left side of the screen. Preceding each presentation of this arrow by 1,000 msec one of two command words, "SIDE" or "DIRECTION," appeared on the screen. This command word served to signal the participant to respond by pressing a key on the side of the keyboard corresponding either to the side of the screen on which the arrow appeared or the direction in which the arrow was pointing. On 50% of the presentations, the side of the screen on which the arrow appeared and the direction in which it was pointing agreed. On the remaining presentations, these two stimulus characteristics were in conflict. Throughout the test, the non-conflict and conflict presentations occurred in a random sequence. Overall, this section of the test included eight practice and 48 test presentations of the command-stimulus combination. Data selected for study analyses included the total correct and total incorrect responses for each participant on each SAT trial.

Following each administration of the performance testing and Stanford Sleepiness Scale, the participant was placed in a laboratory bedroom for the MSLT trial. Most aspects of the

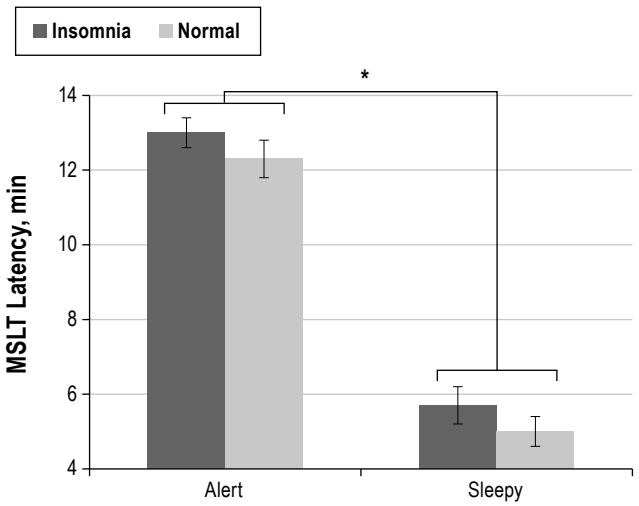

Figure 1—Mean MSLT latencies (min) of alert and sleepy participants. MLST, Multiple Sleep Latency Test. *Indicates group differences by a posteriori comparisons.

standard protocol[27] were followed in conducting the MSLT. However, conservative MSLT criteria rather than contemporary clinical criteria were used to define the sleep latency for each nap. Specifically, sleep latency was defined as the time between the beginning of the nap trial and either the first three consecutive 30-sec epochs of stage 1 sleep or the first 30-sec epoch of any other sleep stage. If no sleep occurred, the trial was terminated at 20 min and a sleep latency of 20 min was assigned. To minimize carryover effects from one nap to the next, each nap trial was discontinued once the sleep onset criterion was met.

Psychometric Testing

Participants completed the State-Trait Anxiety Inventory[28] along with a variety of other psychometric measures as per requirements of the parent study. For the purpose of this investigation, participants' scores on the Trait section of this inventory were retained to provide a corroborating index of their arousal levels.

Statistical Analyses

Because MSLT sleep latencies have been used as an index of physiological hyperarousal in individuals with insomnia, we first computed each participant's mean sleep latency across MSLT trials. We then subdivided our samples of individuals with PI and NS into alert and sleepy groups using the MSLT mean latency cutoff suggested in the International Classification of Sleep Disorders, Second Edition for connoting the type of excessive sleepiness as found in hypersomnolent patients such as those with narcolepsy. Specifically, participants with PI and NS with mean MSLT latencies ≤ 8 min were classified as sleepy, whereas the remaining participants were classified as alert.

Following this classification process, we conducted a series of preliminary 2 (PI versus NS) × 2 (alert versus sleepy) factorial analyses to compare the various subgroups in regard to their mean MSLT latencies and Stanford Sleepiness Scale scores across trials as well as in regard to their mean values of TST, SOL, WASO, and SE derived from the 3 nights of PSG conducted prior to their daytime testing. We conducted a similar analysis to compare the subgroups on Trait Anxiety Scale scores.

For the purpose of the main study analyses, we computed the mean number of correct responses as well as the mean number of error responses made on both the CPT and SAT across trials by each participant. Because plots of these data showed neither the mean numbers of correct responses nor errors were normally distributed, we performed arithmetic normalizing operations with these data to make them acceptable for parametric analyses. Finally, we conducted separate 2 (PI versus NS) × 2 (alert versus sleepy) analyses of covariance (ANCOVAs) with the normalized values of these correct and error response data to address the main study questions. Preliminary ANCOVAs were conducted with a range of covariates known to influence performance testing results including age, sex, years of education, body mass index (BMI), and mean values of the AHI and periodic limb movement-Arousal Index derived from the 3 nights of PSG prior to daytime testing. A final set of ANCOVAs were then conducted using only those covariates found to account for significant portions of the variance in the statistical models. Because these primary study analyses included two separate dependent measures, we used a Bonferroni adjusted alpha level (0.05 ÷ 2 = 0.025) to control for experimenter-wise error in assigning statistical significance to our results. All ANCOVAs were conducted using the PROC GLM procedure in version 9.2 of the Statistical Analysis System (SAS Institute, Inc, Cary, NC) software.[29]

RESULTS

Classification Results

Use of the mean MSLT latencies to identify alert and sleepy participants resulted in 53 individuals with PI (26 women) and 42 NS (27 women) classified as alert and 36 individuals with PI (22 women) and 53 NS (21 women) categorized as sleepy. Chi-square analyses showed the four subgroups did not differ in their sex compositions (χ^2 (3) = 7.17, P = 0.07) nor in regard to their proportions of individuals sleeping in their homes versus the sleep laboratory prior to their daytime testing (χ^2 (3) = 5.73, P = 0.13. However, a 2 (PI versus NS) × 2 (alert versus sleepy) analysis of variance (ANOVA) showed those participants comprising the sleepy group were significantly younger than were those comprising the alert group (45.8 versus 51.2 y; F [1, 180] = 4.59, P = 0.03). A similar ANOVA showed the subgroups did not differ in regard to their educational levels (F [1, 180] = 0.63, P = 0.43).

Preliminary Analyses

We conducted an initial set of analyses to test the effectiveness of study procedures for discriminating the alert and sleepy subgroups and to compare these subgroups in terms of their PSG-derived sleep measures and subjective measures of daytime sleepiness and general arousal. For our first analyses, we conducted a 2 (PI versus NS) × 2 (alert versus sleepy) ANCOVA in which each participant's mean MSLT sleep latency across trials served as the dependent measure. Because our sleepy groups were found to be significantly younger than our alert groups, we included age as a covariate in this analysis. Results of this analysis showed a significant (F [1, 179] = 266.96, P = 0.0001) main effect for the comparison of the alert and sleepy groups. Figure 1 shows mean MSLT latencies for both the PI and NS comprising each of these two groups. This figure along with the statistically

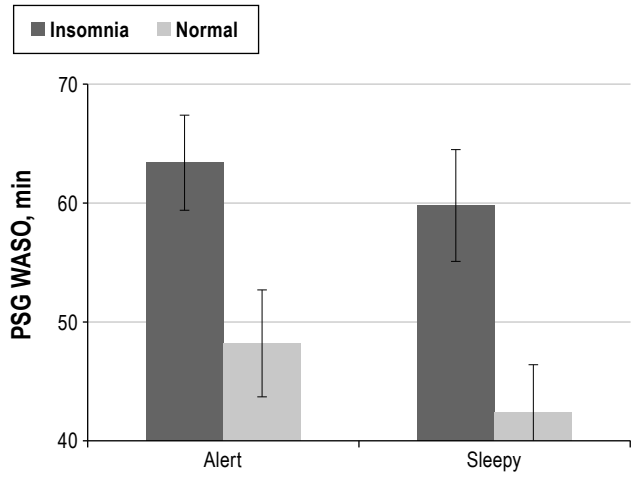

Figure 2—PSG mean WASO (min) across three recording nights. PSG, polysomnography; WASO, wake after sleep onset.

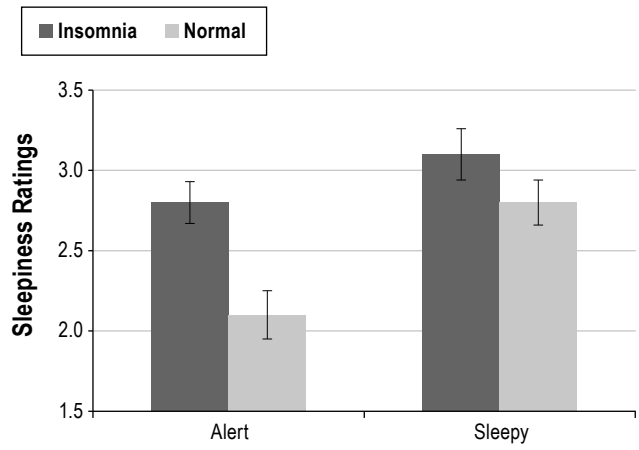

Figure 4—Mean Stanford Sleepiness Scale ratings across daytime testing trials.

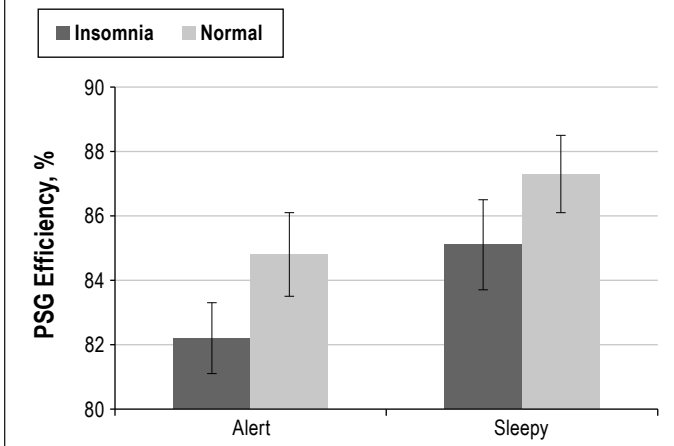

Figure 3—PSG mean sleep efficiency (%) across three recording nights. PSG, polysomnography.

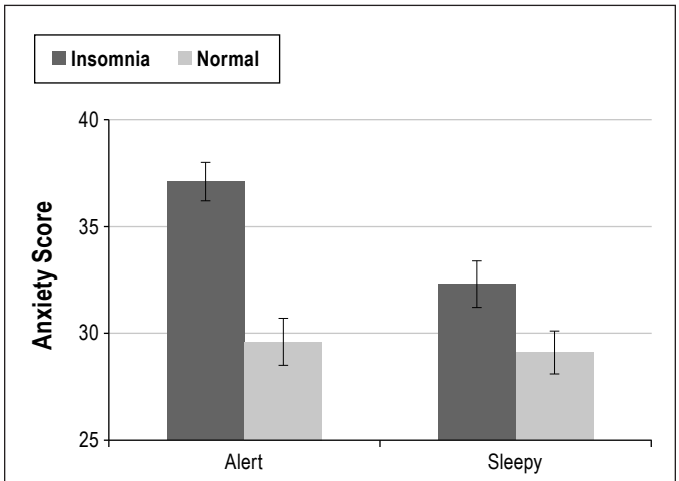

Figure 5—Anxiety scores on trait section of the State-Trait Anxiety Inventory.

significant main effect observed suggested our classification procedure was very effective in discriminating alert individuals from those with significant levels of daytime sleepiness.

Age-adjusted 2 (PI vs. NS) × 2 (alert versus sleepy) ANCOVAs conducted to compare our subgroups in regard to PSG measures, sleepiness ratings, and Trait Anxiety scores showed main or interaction effects for PSG-derived WASO and SE, the subjective sleepiness ratings, and Trait Anxiety scores. Figures 2 through 5 provide comparisons of subgroup means across these measures. Analyses of PSG measures showed the PI group collectively had significantly higher mean values of WASO than did the NS (61.6 versus 45.3 min; F [1, 177] = 14.74, P = 0.0002), whereas the participants classified as alert had significantly lower mean sleep efficiencies than did those classified as sleepy (83.4% versus 86.3%, F [1,177] = 5.10, P = 0.03) across the 3 nights of sleep monitoring. However, as noted by Figures 3 and 4, the alert PI group had the highest mean values of WASO and lowest mean SEs, suggesting the greatest degree of sleep disturbance in this group. The analyses of Stanford Sleepiness Scale scores showed the individuals with PI collectively rated themselves as significantly sleepier than did the NS (2.9 versus 2.4, F [1, 178] = 11.2, P = 0.001) and all of those classified as sleepy rated themselves as sleepier than did those classified as alert (2.9 versus 2.5, F[1, 178] = 7.45, P = 0.007). Finally, the analysis of the Trait Anxiety scores showed a significant interaction between participant type and alertness level (F [1, 176] = 4.89, P = 0.03). *A posteriori* contrasts were conducted with the LSMEANS procedure in the SAS software. This procedure provides predicted group means adjusted for all covariates in the statistical model. Results of these comparisons showed the alert individuals with insomnia had significantly higher scores on this scale than did the remaining three groups. These latter findings coupled with their MSLT performances and PSG findings imply a 24-h physiological hyperarousal pattern in the alert PI subgroup.

Performance Testing Results

A small subset of the sample (n = 7 [3.8%]) had missing data for some of the covariates (e.g., education level, BMI) used in the preliminary ANCOVAs planned and, thus, were excluded from these analyses. Results of these analyses, which adjusted for age, years of education, sex, race, mean AHI, and mean periodic limb movement-Arousal Index, showed a significant main

Table 2—Means, standard deviations, and statistical results for primary performance testing dependent measures

Dependent Measure	Alert		Sleepy		F and P values for statistical tests		
	Insomnia	Normal sleepers	Insomnia	Normal sleepers	Subject type 1	Alertness group 2	1 × 2
Mean correct responses	75.7[a] (4.4)	77.5[b] (2.4)	76.5[a] (2.6)	77.7[b] (2.0)	F = 9.77 P = 0.0021	F = 0.41 P = 0.52	F = 1.86 P = 0.17
Mean errors	4.5[a] (3.6)	2.6[b] (1.9)	3.2[a,b] (2.5)	4.4[a] (4.4)	F = 0.25 P = 0.61	F = 0.64 P = 0.42	F = 10.7 P = 0.0013

Means marked with the same superscript letter (a, b) were not found to be significantly different from each other in *a posteriori* contrasts.

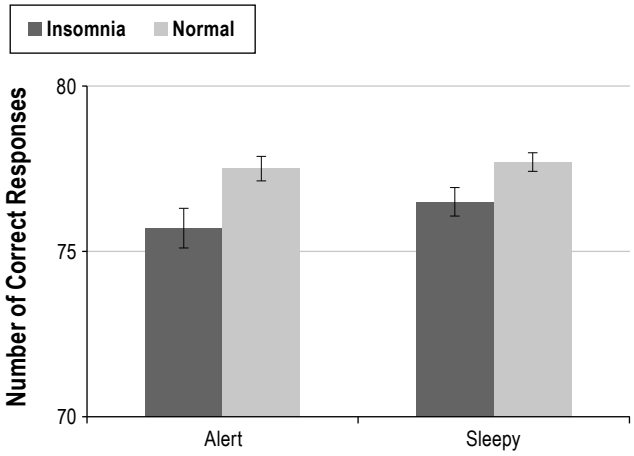

Figure 6—Mean number of correct responses across testing trials.

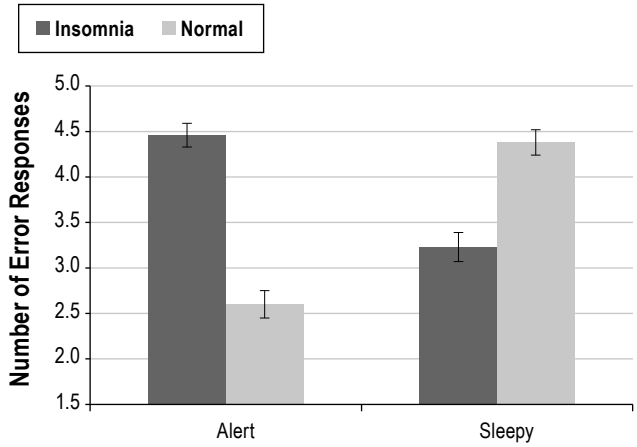

Figure 7—Mean number of error responses across testing trials.

effect (F [1,166] = 9.48, P = 0.0024) for participant type in the analysis of the correct response rates and a significant participant type × alertness level interaction effect (F [1, 166] = 8.30, P = 0.0045) in the analysis of the error rate data. Because BMI, sex, mean AHI, and mean periodic limb movement-Arousal Index did not account for significant portions of the variance in either of these analyses, they were excluded from the models and a final set of ANCOVAs were conducted with the remaining covariates. None of the participants had missing data for the remaining covariates so the final set of ANCOVAs included the total study sample. Results of these final analyses corroborated the results of the preliminary ANCOVAs and showed a significant main effect (F [1,176] = 9.77, P = 0.0021) for participant type in the analysis of the correct response rates and a significant participant type × alertness level interaction effect (F [1, 176] = 10.68, P = 0.0013) in the analysis of participants' error rates. The remaining main and interaction effects tested in these two models were not statistically significant (P values ranging from 0.17 to 0.61). Table 2 shows raw means and standard deviations of the subgroups' correct and error responses, whereas Figures 6 and 7 show the means and standard error terms for these data graphically. To decompose the significant interaction term found in the analysis of participants' error rates, we conducted *a posteriori* contrasts using the LSMEANS procedure included in the SAS software. This procedure was chosen because it provides all possible paired comparisons of the four subgroups involved in the interaction term and it adjusts the means involved in these comparisons for all covariates included in the ANCOVA model. Because this procedure provided a total of six paired comparisons, we used a Bonferroni-adjusted alpha = 0.008 (0.05 ÷ 6) to assign significance to the mean differences observed. Results of these comparisons are summarized in Table 2. As shown there, the alert PI participants logged significantly (P = 0.006) more errors on average across trials than did the alert NS. Whereas the alert NS showed a significantly lower (P = 0.004) error rate than did the sleepy NS, they did not differ significantly (P = 0.06) from the sleepy PI group in their error rates across trials. Likewise, the differences noted between the alert and sleepy PI participants did not reach statistical significance (P = 0.08).

DISCUSSION

The current study was conducted to assess the effects of physiological hyperarousal on the neurocognitive performances of individuals with PI. We were mainly interested in discerning whether individuals with PI with evidence of physiological hyperarousal might be either protected from or vulnerable to daytime neurocognitive deficits associated with their insomnia disorders. Overall, our results suggest that physiological hyperarousal impairs rather than facilitates the cognitive performances of individuals with PI, at least as measured by their correct and error response rates on the reaction time tests we used. Our hyperaroused PI participants logged fewer correct responses and made more errors on reaction time tasks than did the similarly alert group of NS. Moreover, whereas the sleepy group of NS appeared as error-prone as the hyperaroused PI group, the latter group logged significantly fewer correct responses than did the former. Thus, of the various subgroups considered, our

physiological hyperaroused PI group seemed the most disposed to poor test performances. These results, in turn, support the notion of Vgontzas et al.[13] and Fernandez-Mendoza et al.[14] that individuals with PI with a physiological hyperarousal trait have more cognitive dysfunction than individuals with PI with lower arousal levels.

This study complements and extends our previous report[9] wherein we showed that individuals with insomnia have slower and less consistent reaction times on complex tasks than do NS. The current findings suggest that individuals with PI also show deficits in response accuracy and particularly so if they manifest a pattern of physiological hyperarousal. The deleterious effects of this form of hyperarousal on performance among individuals with PI perhaps is not surprising when considering what is known about human performance and arousal. As early as 1908, Yerkes and Dodson[30] noted that human performance increases with physiological or mental arousal, but only up to a point. When levels of arousal become too high, performance decreases, particularly when complex tasks are considered.[31]

Although not the primary focus of the study, our results also highlight the relative performance deficits shown by NS who have both objective and subjective evidence of daytime sleepiness. Our sleepy normal group rated themselves about as sleepy as our alert (physiologically hyperaroused) PI group, but unlike this PI group they also had mean MSLT latencies implying excessive daytime sleepiness. However, this sleepy NS group made about as many errors on performance testing as did the physiologically hyperaroused PI group. These findings are consistent with those of Bonnet and Arand,[10] who found that NS who show both objective and subjective sleepiness also show poorer performances on daytime vigilance testing than do either objectively alert NS or objectively sleepy NS who view themselves as being alert. Hence, as suggested by these authors, NS who are objectively and subjectively sleepy in the daytime may have some reduced ability to maintain normal physiological arousal.

The association between physiological hyperarousal and error rates noted among our PI group herein complements epidemiological studies[32,33] that have shown increased risks for work and traffic accidents among those with insomnia complaints. The results also add to a growing body of literature suggesting the deleterious cardiovascular and neurocognitive effects of physiological hyperarousal among those with insomnia.[12,13] Whereas a number of past studies did not show differences between PI and NS groups on neurocognitive tests, we suspect that the types of tests used for such comparisons may determine whether or not group differences are found. Our previous[9] and current findings fit well with those of Fernandez-Mendoza et al.[12] in suggesting complex tasks such as switching attention tests are particularly sensitive for revealing the daytime impairment of the physiologically hyperaroused PI group. Thus, future studies of this nature may benefit by the use of these types of tests when conducting such group comparisons.

Our current findings, as well as those of Vgontzas' group.[12-14] suggest that it is important to discriminate those with and without physiological hyperarousal when examining the daytime impairments of those with PI. It should be noted that the manner in which we and others identified physiologically hyperaroused insomnia sufferers differed somewhat. Vgontzas et al.[13] and Fernandez-Mendoza et al.,[14] for example, characterized individuals with insomnia with a persistent pattern of short sleep as most prone to physiological hyperarousal. In contrast, we used daytime MSLT mean sleep latencies to identify those individuals with PI with such a hyperarousal pattern. Nonetheless, we would expect these two approaches to produce relatively similar results because there are ample data to show that individuals with PI with shorter nocturnal sleep durations tend to have longer MSLT latencies and show higher levels of daytime vigilance than do those with normal sleep durations.[1,7,8,34-37] Although we did not find differences in sleep duration between our hyperaroused and presumably nonaroused PI subgroups across the 3 nights of PSG, methodological factors could explain these results. Prior studies using short objective sleep duration for identifying physiologically hyperaroused individuals with PI used laboratory PSG methods with study participants afforded standardized and fixed times in bed. In contrast, participants in the current study followed *ad libitum* bed and rising times and a portion of the sample slept in their homes prior to daytime testing. These factors may account for our failure to find difference in nocturnal sleep duration between our alert and sleepy PI groups. However future studies using our MSLT assay along with laboratory PSG and fixed recording periods are needed to confirm this assumption.

However, it is worth noting that both our current and previous findings do suggest an association between objective sleep disturbance and daytime performance among those with PI. In our prior study[9] we found that values of WASO and SE derived from nocturnal PSG were predictive of average reaction time performances on subsequent daytime testing in individuals with PI. Specifically, poorer performances were associated with higher values of WASO and lower values of SE. In the current study, we examined participants' correct and error response rates instead of reaction times and once again found similar associations between WASO and SE and the daytime performances of our study participants. Our physiologically hyperaroused insomnia group, which showed the fewest correct responses and highest error rate on average, also had the highest values of WASO and lowest values of SE on the PSGs. Hence, objective sleep disturbance appears to relate to the daytime performance deficits of our PI group and particularly those with evidence of physiological hyperarousal.

Admittedly, this study had a number of limitations that deserve mentioning. The PI group consisted of thoroughly screened research volunteers. As such, results may not generalize to clinical samples. Our definition of physiological hyperarousal was based solely on one MSLT and lacked any more direct physiological corroborative measures of arousal. Although group comparisons using measures derived from PSG and the Trait Anxiety Scale suggest our hyperaroused group was indeed hyperaroused, more direct physiological measures to confirm that assumption would have been desirable. In addition, we used a very limited number and type of performance tests. It is possible that other types of neurocognitive measures would provide more insight into the diurnal impairments endured by hyperaroused individuals with PI. Finally, although we screened all enrollees with PSG to rule out sleep apnea, our recording montage did not include the array of respiratory indices usually employed in diagnostic PSGs. Consequently, it

is possible that some of our participants suffered from occult sleep disordered breathing that contributed to their performances deficits. Thus, replications of this study with individuals with clinical insomnia, physiological confirmation of hyperarousal, a wider range of performance measures, and more comprehensive PSG recordings may be useful. Nonetheless, our results suggest a significant association between error rates and physiological hyperarousal among those with chronic PI.

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