NEW RESEARCH

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Number of Lapses during the Psychomotor Vigilance Task as an Objective Measure of Fatigue

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SCIENTIFIC INVESTIGATIONS

Purpose: This study examined how well the Psychomotor Vigilance Task (PVT) performance was related to subjective measures of fatigue. In order to study subjects presenting with a wide range of fatigue symptoms, we studied healthy individuals as well as patients with varying severity of obstructive sleep apnea. We also examined if the PVT/fatigue relationship could be influenced by depressive symptoms.

Subjects and Methods: Forty-eight participants had their sleep monitored with polysomnography. Fatigue was assessed by Multidimensional Fatigue Symptom Inventory-short form (MFSI-sf). Depressed mood was assessed by the Center for Epidemiologic Studies-Depression (CES-D) Scale. After sleep monitoring and psychological assessments, the 10-minute PVT was administered. The main outcome variable was the PVT lapse count. Simple correlations and hierarchical linear regression were used to examine the association between age, body mass index (BMI), sleep variables, apnea hypopnea index (AHI), oxygen desaturation index (ODI), CES-D, fatigue, and PVT.

Results and Conclusion: The PVT lapse count was significantly associated with MFSI-sf physical fatigue ($r = 0.324$, $p = 0.025$). In hierarchical regression (full model $R^2 = 0.256$, $p = 0.048$), higher BMI ($p = 0.038$), and higher MFSI-sf physical fatigue ($p = 0.040$) were independent predictors of the PVT lapse count. Age, AHI, ODI, and CES-D were unrelated to the PVT lapse count. In conclusion, the findings suggest that even after controlling for age, BMI, depression, and apnea severity, physical fatigue is associated with the PVT lapse.

Keywords: Psychomotor Vigilance Task, fatigue, Multidimensional Fatigue Symptom Inventory-short form, obstructive sleep apnea

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The study of fatigue has grown in recent years, but researchers still need to rely on subjective reports as there is no objective measure available. Fatigue has a complex nature and may manifest in a wide range of symptoms, including behavioral, cognitive, somatic, and affective. Increasingly, investigations have developed multidimensional instruments to capture the full spectrum of the fatigue symptom profile. The Multidimensional Fatigue Symptom Inventory (MFSI) has been widely used for measuring subjective fatigue.[1] This scale examines 5 different components of fatigue consists of general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor.[2]

Fatigue is a common symptom of depression and many studies have reported a significant positive relationship between fatigue and depression.[3-5] Moreover, Bardwell and colleagues demonstrated that, after severity of obstructive sleep apnea (OSA) was controlled, higher levels of depressive symptoms were independently associated with a greater level of fatigue.[5,6]

Although fatigue is not synonymous with daytime sleepiness and may or may not be a function of sleep loss,[7,8] there are several objective parameters such as electroencephalography (EEG),[9] event-related potential,[10] and electrocardiogram[11] which have been used as indicators of drowsiness, and at times, fatigue. However, these methods have generally been regarded as impractical or of limited value.

Various psychomotor tests have also been used to assess fatigue and performance. The psychomotor vigilance task (PVT) has been demonstrated to be sensitive to sleep disruption and is regarded as an objective indicator of cognitive impairment in a variety of experimental conditions such as partial sleep loss,[12,13] chronic sleep restriction,[14-16] napping,[17,18] and sleepiness.[19] Other studies have found that the PVT is correlated with objective measures of sleepiness, including the multiple sleep latency test, in studies of partial sleep deprivation and in OSA patients.[15,20] In addition to studies of PVT results in sleep loss, recent studies have suggested that the PVT performance may also be a good marker of fatigue.[21,22] The PVT maybe a practical instrument to assess fatigue because of its objectivity. In addition, an objective measure of fatigue can be employed with non-English speaking patients.

The PVT is a computer-based test that uses a reaction time paradigm. Subjects are told to press a key in response to a digital signal on a computer terminal. Lapses, defined as a failure to react or any reaction exceeding 500 msec, are often used as the primary outcome measures of PVT performance.[23] The PVT lapse is a hallmark of a sleep-deprived state and is a highly sensi-

BRIEF SUMMARY

Current Knowledge/Study Rationale: Objective markers of fatigue are scarce. This study determined if the PVT functions as an adequate proxy for fatigue and how depressive symptoms affect that relationship in normals and patients with OSA.

Study Impact: PVT lapse is associated with physical fatigue symptoms. Furthermore, that relationship is independent of depressive symptoms or measures of apnea severity.

tive measure of the effects of sleep deprivation, or sleep restriction, on attention and vigilance.[15,24,25] The mechanism of these lapses has been thought to result from perceptual, processing, or executive failures in the central nervous system. Sleep deprivation amplifies the tendency of this system to fail.[23] Another PVT measure, the PVT count of false responses (responding with no stimulus is presented, lack of behavior inhibition) is thought to reflect impaired executive functioning.[26]

Vigilance and sustained attention as measured by the PVT performance values are decreased in obstructive sleep apnea (OSA).[27] The PVT performance decline has been shown to be associated with higher BMI,[27] older age,[28] female gender,[29] more sleep loss (total sleep deprivation, chronic partial sleep restriction, and sleep fragmentation),[15,30] and higher apnea hypopnea index (AHI).[27] This study examined how well PVT performance (i.e., lapse and average reaction time) was related to various subscales of the MFSI-sf. In order to study subjects presenting with a wide range of fatigue symptoms, we studied healthy individuals as well as patients with obstructive sleep apnea. Given the association of depression with fatigue,[6,31-33] we also examined if the PVT-fatigue relationship could be influenced by depressive symptoms. Our hypotheses were: (1) PVT performance would be worsened in the setting of increased age, BMI, OSA severity (AHI and ODI), depression (CES-D), and level of subjective fatigue (MFSI-sf). (2) After controlling demographic factors (age and BMI), OSA severity (AHI and ODI), and depression (CES-D), PVT performance could be predicted by fatigue level. (3) PVT performance could be an objective measure of specific domains of subjective fatigue.

METHODS

Participants

Ten women and 39 men were studied as part of a larger protocol examining physiological abnormalities in patients with and without obstructive sleep apnea. Participants' mean age was 49.2 ± 9.4 years, and mean BMI was 29.7 ± 5.5. They were well educated (mean years of education 15.6 ± 2.7 years) and were recruited by advertisement and word-of-mouth referral. Participants were excluded if they reported a history of major medical illnesses (other than OSA and hypertension), if they had a current psychiatric diagnosis, were receiving psychotropic or sedative hypnotic medication, or were receiving treatment for OSA. Patients who were receiving antihypertensive medications had their medications tapered for 3 weeks before participation. One subject was excluded because her score on the PVT lapse was > 2.5 standard deviations from the mean, leaving 48 subjects in the analysis. The protocol was approved by the University of California San Diego (UCSD) Human Subjects Committee, and all participants provided written informed consent.

Procedure

Participants were admitted to the UCSD General Clinical Research Center Gillin Laboratory of Sleep and Chronobiology at 17:00 for psychological assessment (i.e., CES-D, MFSI, and Marlowe-Crowne Social Desirability scale). On their second night in the hospital, participants had their sleep monitored from 22:00 to 06:00. Following the sleep study, behavioral alertness was assessed at 10:00.

Sleep Monitoring

Sleep was monitored with the Grass Heritage digital polysomnograph (Model PSG36-2, Astro-Med, Inc., West Warwick, RI, USA). Central and occipital electroencephalogram, bilateral electrooculogram, submental and tibialis anterior electromyogram, electrocardiogram, body position, nasal airflow using a nasal cannula–pressure transducer, and naso-oral airflow using a thermistor were assessed. Respiratory effort was measured using chest and abdominal piezoelectric belts. Sleep records were manually scored according to the criteria of Rechtschaffen and Kales.[34] Apneas were defined as decrements in airflow ≥ 90% from baseline for ≥ 10s. Hypopneas were defined as decrements in airflow of ≥ 50% but < 90% from baseline for ≥ 10s. The numbers of apneas and hypopneas per hour were calculated to obtain the apnea hypopnea index (AHI). Participants with an AHI ≥ 10 were considered to have OSA. Oxyhemoglobin saturation was monitored with a pulse oximeter (Biox 3740, Datex-Ohmeda, Louisville, CO) and analyzed using Profox software (Associates, Escondido, CA). The pulse oximeter yields an oxygen desaturation index (ODI) which is the average number of oxygen desaturations at least 3% below baseline level per hour. ODI > 5 is suggestive of OSA.[35] AHI or ODI were taken as indicators of OSA severity.

Fatigue and Depressed Mood Assessments

The Multidimensional Fatigue Symptom Inventory-short form (MFSI-sf)[2] is a 30-item self-report measure designed to assess the principal manifestations of fatigue, yielding a total fatigue score and subscale scores for general fatigue, physical fatigue, emotional fatigue, mental fatigue, and vigor. Items are rated on a 5-point Likert scale indicating how true each statement was for the respondent during the previous week (0 = not all; 4 = extremely). A total fatigue score is calculated by adding the scores for the 4 fatigue subscales and subtracting the score for vigor with a full range from −24 to 96. Thus, in the case of low fatigue and high vigor, total score can be negative. MFSI-sf total scores > 0.85 are considered to be a significant indicator of fatigue.[36]

The Center for Epidemiologic Studies-Depression (CES-D) Scale[37] is a 20-item self-report scale that has been shown to be reliable and valid for assessing depressive symptoms. CES-D scores of ≥ 16 are considered indicative of depressed mood. The CES-D primarily taps cognitive/affective aspects of depression and has been shown to be useful in chronically ill groups, including obstructive sleep apnea patients. The participants are instructed to fill out the CES-D according to how they have felt in the past year.

The Marlowe-Crowne Social Desirability scale[38] was used to assess the impact of social desirability on self-report measures. This measure contains 33 true-false items that describe both acceptable but improbable behaviors, as well as those deemed unacceptable but probable. Persons with high scores on the Marlowe-Crowne Social Desirability scale tend to overreport socially desirable and underreport socially undesirable information about themselves.[39]

Psychomotor Vigilance Performance

Vigilance was assessed with the Psychomotor Vigilance Test (PVT), a 10-minute computerized visual reaction-time task that evaluates sustained attention.[40] Participants were instructed to respond to the appearance of a visual stimulus by pushing a response button as quickly as possible. The stimulus was a red light emitting diode displaying time in milliseconds in a window of the portable PVT-192 device (Ambulatory Monitoring, Inc., Ardsley, NY). During each 10-min session, visual stimuli appeared at variable intervals of 2–10 s. From each PVT trial, reaction times (RTs) were collected and 2 performance variables, average response time and number of lapses (i.e. failure to respond or RT > 500 msec), were extracted using a software program.

Statistical Analysis

Fisher exact test, student *t*-test, and Mann-Whitney U-test were employed to examine differences between normal and apneic group.

In order to account for multiple comparisons due to the multiple fatigue and sleep variables, we applied Fisher's least significant difference test.[41] This is a 2-stage test; in the first stage, the grand null hypothesis encompassing all the hypotheses of interest is tested. If this grand null is rejected, then the second stage tests the individual hypotheses separately.To this end, we first performed a multivariate analysis of variance (MANOVA) using PVT variables as dependent variables (DVs) with demographic variables, sleep parameters (AHI, ODI, percent of stages of sleep, etc.), MFSI-sf subscales, and CES-D. The *F*-test for this MANOVA was statistically significant, hence we proceeded to the second stage and tested individual hypotheses. Pearson correlation analysis was performed to examine how the 2 PVT performance variables were associated with demographic variables, sleep variables, and psychological variables. Hierarchical linear regression analysis was performed using both PVT average response time and count of lapses as the DVs. Step 1 forced entry of age and BMI; step 2 forced entry of OSA severity variables AHI and ODI; step 3 forced entry of CES-D; and step 4 forced entry of MFSI-sf physical fatigue subscale. We only included MFSI-sf physical fatigue in this model because it was the one fatigue subscale that was significantly correlated with PVT lapses in the univariate analysis. Data were analyzed using SPSS 15.0 software (Chicago, IL, 2006). Statistical significance was set at $p < 0.05$.

RESULTS

Sample characteristics with means and standard deviations are presented in **Table 1**. Of the 48 participants, 83.3% had OSA (AHI ≥ 10), 56.2% reported significant fatigue (score > 0.85), and 22.9% reported depressed mood (CES-D score > 16). There were significant group differences in gender, AHI, ODI, stage 1 sleep%, and slow wave sleep%. But there were no significant differences in MFSI-sf, CES-D, and PVT performance between the normal and apneic groups.

The Marlowe-Crown Social Desirability scale was not associated with any of the psychological variables.

Table 2 summarizes the Pearson correlation coefficients between the 2 PVT variables (i.e., count of lapses and average response time) and the other variables of interest. The PVT count of lapses was significantly associated with MFSI-sf physical fatigue ($r = 0.324$, $p = 0.025$). The PVT average response time tended towards a positive correlation with MFSI-sf physical fatigue ($r = 0.281$, $p = 0.053$). There was a significant association between years of education and PVT average response time ($r = -0.428$, $p = 0.005$).

Table 3 presents results of the hierarchical multiple linear regression analysis using PVT count of lapses as the DV. The full model accounted for 25.6% of variance in the DV

Table 1—Sample characteristics (N = 48), Mean (± SD).

Variables	Normal Subjects (AHI < 10, N = 8)	Apneic Subjects (AHI ≥ 10, N = 40)	p value
Demographic Variables			
Gender			
Male	4	35	0.031*
Female	4	5	
Race			
White	5	35	0.116
Black	3	5	
Age (years)	49.50 (9.23)	49.15 (9.51)	0.924
BMI (kg/m^2)	28.68 (5.26)	29.85 (5.56)	0.734
Education (years)[a]	14.83 (4.02)	15.72 (2.46)	0.619
Sleep Variables			
AHI (events/h)	5.19 (3.05)	32.87 (21.16)	< 0.001*
ODI (events/h)	3.59 (2.24)	21.88 (22.59)	< 0.001*
Average Oxygen Saturation	95.00 (1.29)	92.03 (15.12)	0.596
Sleep Stage (%)			
Stage 1	8.08 (2.55)	13.68 (9.39)	0.040*
Stage 2	57.58 (4.91)	55.17 (10.69)	0.331
Slow Wave Sleep	8.68 (7.33)	12.13 (10.69)	0.523
REM	25.69 (5.54)	19.03 (6.65)	0.011*
PVT Variables			
Count of Lapses (Response Time > 500 msec)	2.63 (3.46)	1.75 (2.46)	0.615
Average Response Time (msec)	288.01 (52.33)	264.78 (42.85)	0.213
Psychological Variables			
CES-D	12.50 (8.02)	11.23 (9.14)	0.523
Marlowe-Crowne Social Desirability Scale[b]	21.50 (5.63)	18.18 (6.58)	0.283
MFSI (Short Form) Total	−3.63 (8.02)	7.45 (16.74)	0.076
MFSI (Short Form) Subscales			
General Fatigue	4.00 (3.74)	8.00 (6.23)	0.107
Physical Fatigue	2.63 (1.51)	3.53 (3.71)	0.946
Emotional Fatigue	2.38 (2.56)	3.85 (3.73)	0.268
Mental Fatigue	2.25 (1.83)	4.60 (3.56)	0.069
Vigor	14.88 (3.68)	12.53 (4.59)	0.107

OSA, obstructive sleep apnea; BMI, body mass index; AHI, apnea hypopnea index; ODI, oxygen desaturation index; REM, rapid eye movement sleep; CES-D, Center for Epidemiologic Studies Depression Scale; MFSI, Multidimensional Fatigue Symptom Inventory
[a]N = 42; [b]N = 46; *p < 0.05

Table 2—Univariate correlations (N = 48).

Correlation of PVT Variables with:	Count of Lapses		Average Response Time	
	r	p value	r	p value
Age (Years)	0.026	0.861	0.056	0.707
Bmi (kg/m^2)	0.188	0.201	0.253	0.083
Education (years)[a]	−0.149	0.346	−0.428	0.005*
AHI (events/h)	−0.024	0.874	0.104	0.480
ODI (events/h)	−0.093	0.529	−0.017	0.908
Average Oxygen Saturation (%)	−0.114	0.329	−0.216	0.140
Sleep Stage (%)				
Stage 1	−0.035	0.812	0.070	0.638
Stage 2	0.235	0.108	0.041	0.784
Slow Wave Sleep	−0.147	0.317	−0.154	0.295
REM	−0.076	0.606	0.081	0.585
CES-D (Long Form)	0.169	0.252	0.249	0.088
MFSI (Short Form) Total	0.144	0.329	0.154	0.297
MFSI (Short Form) Subscales				
General Fatigue	0.069	0.640	−0.001	0.994
Physical Fatigue	0.324	0.025*	0.281	0.053
Emotional Fatigue	0.129	0.382	0.157	0.285
Mental Fatigue	−0.042	0.775	−0.010	0.944
Vigor	0.139	0.345	−0.180	0.222

BMI, body mass index; AHI, apnea hypopnea index; ODI, oxygen desaturation index; REM, rapid eye movement sleep; CES-D, Center for Epidemiologic Studies Depression Scale; MFSI, Multidimensional Fatigue Symptom Inventory
[a] N = 42
*p < 0.05

Table 3—Multiple regression predictors of PVT count of lapses.

	R^2	Adjusted R^2	Variables	β	p value
Step 1[a]	0.039	−0.004	Age	0.061	0.683
			BMI	0.199	0.188
Step 2[b]	0.158	0.080	Age	0.076	0.597
			BMI	0.503	0.014
			AHI	0.353	0.287
			ODI	−0.752	0.041
Step 3[c]	0.175	0.077	Age	0.093	0.524
			BMI	0.471	0.022
			AHI	0.300	0.373
			ODI	−0.723	0.050
			CES-D	0.141	0.360
Step 4[d]	0.256	0.148	Age	0.063	0.656
			BMI	0.414	0.038
			AHI	0.167	0.611
			ODI	−0.677	0.057
			CES-D	0.018	0.909
			MFSI (short form)-Physical Fatigue	0.354	0.040

BMI, body mass index; AHI, apnea hypopnea index; ODI, oxygen desaturation index; CES-D, Center for Epidemiologic Studies Depression Scale; MFSI, Multidimensional Fatigue Symptom Inventory
[a] $F_{2,45}$ = 0.911, p = 0.410, R^2 change 0.039
[b] $F_{4,43}$ = 2.022, p = 0.108, R^2 change 0.119
[c] $F_{5,42}$ = 1.784, p = 0.137, R^2 change 0.017
[d] $F_{6,41}$ = 2.356, p = 0.048, R^2 change 0.081

(F = 2.356, p = 0.048). In step 1, age and BMI did not account for a significant amount of variance (R^2 = 0.039, p = 0.410). The model at step 2, which included AHI and ODI in addition to the variables from step 1, was again not significant overall (R^2 = 0.158, p = 0.108). After adding CES-D in step 3, the model was still not significant (R^2 = 0.175, p = 0.137). In step 4, the model became significant overall (p = 0.048), after including MFSI-sf physical fatigue, which accounted for 8% more variance in the PVT count of lapses. In the final model, BMI, and MFSI-sf physical fatigue were significant individual predictors of the PVT count of lapses (p < 0.05). However, age, AHI, ODI, and CES-D were not significant individual predictors.

Table 4 presents results of the hierarchical multiple linear regression analysis using the PVT average response time as the DV. The full model accounted for 27.6% of variance in the DV (F = 2.611, p = 0.031). In step 4, the model was again significant overall (p = 0.031), with the addition of MFSI-sf physical fatigue accounting for an additional 2% of variance in the DV; however, MFSI-sf physical fatigue was not a significant individual predictor (p = 0.324). As significant individual predictors, BMI was positively and ODI was negatively associated with PVT average response time in steps 2 through 4 (p < 0.05). Age, AHI, and CES-D were not significant individual predictors at any step of the analysis.

DISCUSSION

This study examined the relationship between PVT performance (lapse and average response time) and fatigue as measured by various subscales of the MFSI. We demonstrated that the PVT count of lapses was significantly associated with physical symptoms of fatigue (the MFSI-sf physical fatigue). To our knowledge, this study is the first to show the association of MFSI-sf physical fatigue with PVT lapse. The other MFSI-sf subscales (general fatigue, emotional fatigue, mental fatigue, vigor) were not associated with the PVT count of lapses. Furthermore, MFSI-sf physical fatigue trended toward a relationship with the PVT average response time. Thus, these findings also suggest the utility of PVT performance to track specific domains of subjective fatigue.

Our study sample with OSA patients and normal subjects showed a broad range of fatigue symptoms, with approximately 56% self-reporting a significant amount of fatigue. OSA severity (AHI and ODI) was unrelated to the PVT count of lapses and average response time. Previous studies have reported that vigilance impairment is the most common and persistent cognitive finding in OSA patients. While hypoxemia and sleep fragmentation are possible mechanisms of cognitive impairments, we did not find a relationship between OSA severity and PVT performance. Because our sample size was relatively small and

Table 4—Multiple regression predictors of PVT average response time

	R^2	Adjusted R^2	Variables	β	p value
Step 1[a]	0.074	0.033	Age	0.103	0.481
			BMI	0.271	0.069
Step 2[b]	0.230	0.159	Age	0.102	0.461
			BMI	0.544	0.006
			AHI	0.670	0.038
			ODI	−0.989	0.006
Step 3[c]	0.259	0.171	Age	0.124	0.372
			BMI	0.502	0.011
			AHI	0.601	0.064
			ODI	−0.952	0.008
			CES-D	0.185	0.209
Step 4[d]	0.276	0.171	Age	0.110	0.431
			BMI	0.475	0.017
			AHI	0.539	0.101
			ODI	−0.930	0.009
			CES-D	0.127	0.418
			MFSI (short form)-Physical Fatigue	0.165	0.324

BMI, body mass index; AHI, apnea hypopnea index; ODI, oxygen desaturation index; CES-D, Center for Epidemiologic Studies Depression Scale; MFSI, Multidimensional Fatigue Symptom Inventory

[a] $F_{2,45} = 1.809$, p = 0.176, R^2 change 0.074

[b] $F_{4,43} = 3.213$, p = 0.021, R^2 change 0.156

[c] $F_{5,42} = 2.934$, p = 0.023, R^2 change 0.029

[d] $F_{6,41} = 2.611$, p = 0.031, R^2 change 0.018

heterogeneous with wide ranging values of fatigue and apnea severity, our ability to observe a relationship between OSA severity and PVT performance may have been limited.

Higher BMI and higher physical symptoms of subjective fatigue (the MFSI-sf physical fatigue) were independent predictors of the PVT count of lapses. We found that even after controlling for age, BMI, OSA severity, and depression, physical fatigue was associated with PVT lapse. The association of higher BMI with more frequent lapses is consistent with a previous study.[28]

In this study, depressive symptoms were not particularly prominent (mean CES-D score = 11.4) in the group as a whole, but about 23% of our participants scored in the depressed range. Depressive symptoms did not show a negative impact on PVT performance. However, severity of depressive symptoms might not have been high enough to affect vigilant attention performance, and this finding is consistent with a previous study showing that minor depression did not affect cognitive performance.[42] This study demonstrated that PVT lapses tracked subjective reports of fatigue closely, even after controlling depression, apnea severity, and demographic variables. This is an important observation because fatigue research has been hampered by the lack of practical instruments to assess fatigue.

This study has a number of limitations. Surprisingly, ODI was negatively associated with PVT average response time. This suggests that better oxygenation predicts worse cognitive performance, which is counterintuitive. We made a number of attempts to examine this curious finding; however, it does not appear to be the result of outliers, leverage points, or multicollinearity. One possible explanation is that our sample was, on average, fairly well oxygenated. Because ODI counts the number of desaturations that exceed 3%, it is possible for this number to be high even though an individual doesn't drop below 90% saturation.

Because the current study population was limited to OSA patients and normal subjects, the PVT and fatigue relationship should be determined in other groups of patients such as those with chronic fatigue syndrome, anemia, multiple sclerosis, and cancer. Future studies might explore if the PVT and fatigue relationship is affected after treatment of specific disorders such as CPAP treatment in OSA patients and EPO treatment in cancer patients with significant amounts of anemia.

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