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SCIENTIFIC INVESTIGATIONS

CPAP Adherence is Associated With Attentional Improvements in a Group of Primarily Male Patients With Moderate to Severe OSA

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Study Objectives: Obstructive sleep apnea (OSA) is a widespread condition that adversely affects physical health and cognitive functioning. The prevailing treatment for OSA is continuous positive airway pressure (CPAP), but therapeutic benefits are dependent on consistent use. Our goal was to investigate the relationship between CPAP adherence and measures of sustained attention in patients with OSA. Our hypothesis was that the Psychomotor Vigilance Task (PVT) would be sensitive to attention-related improvements resulting from CPAP use.

Methods: This study was a secondary analysis of a larger clinical trial. Treatment adherence was determined from CPAP use data. Validated sleep-related questionnaires and a sustained-attention and alertness test (PVT) were administered to participants at baseline and at the 6-month time point.

Results: Over a 6-month time period, the average CPAP adherence was 3.32 h/night (standard deviation [SD] = 2.53), average improvement in PVT minor lapses was −4.77 (SD = 13.2), and average improvement in PVT reaction time was −73.1 milliseconds (standard deviation = 211). Multiple linear regression analysis showed that higher CPAP adherence was significantly associated with a greater reduction in minor lapses in attention after 6 months of continuous treatment with CPAP therapy (β = −0.72, standard error = 0.34, *P* = .037).

Conclusions: The results of this study showed that higher levels of CPAP adherence were associated with significant improvements in vigilance. Because the PVT is a performance-based measure that is not influenced by prior learning and is not subjective, it may be an important supplement to patient self-reported assessments.

Clinical Trial Registration: Name: Effect of Self-Management on Improving Sleep Apnea Outcomes, URL: https://clinicaltrials.gov/ct2/show/NCT00310310, Identifier: NCT00310310

Keywords: continuous positive airway pressure therapy, obstructive sleep apnea, Psychomotor Vigilance Task, treatment adherence

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INTRODUCTION

Obstructive sleep apnea (OSA) is a widespread, chronic condition characterized by repeated reductions (hypopneas) and/or complete cessations of breathing (apneas) during sleep. Without proper treatment, OSA can lead to a number of adverse physical and psychosocial consequences including hypoxemia,[1] cardiovascular disease,[2] heart failure, increased risk of stroke,[3] excessive daytime sleepiness,[4] depression,[5] and an array of cognitive deficits.[6–8] Continuous positive airway pressure (CPAP) is the most common and efficacious therapy for OSA. CPAP has been demonstrated to safely and effectively manage OSA symptoms with regular long-term use, but therapeutic benefits are dependent on treatment adherence.[9–12]

Despite its demonstrated efficacy at mitigating OSA symptoms, overall rates of CPAP treatment adherence are disappointingly low.[13–16] Considerable research has been carried out to determine ways that CPAP adherence can be increased.[17–19] Although clear predictors of CPAP treatment adherence remain uncertain, studies have provided suggestive evidence that patients with more severe disease (as indicated by a higher apnea-hypopnea index [AHI]) as well as those who report favorable treatment-related outcomes may have a higher likelihood of adhering to long-term treatment.[20,21] Research providing early interventions to patients on CPAP could more clearly identify predictors of successful long-term adherence, which would benefit both patients and providers.[22]

Various forms of cognitive impairment have been attributed to OSA (eg, attention, memory, executive function, and vigilance).[23,24] Methods that can reliably detect and objectively monitor such impairments would be of great utility to clinicians. One relatively simple and straightforward approach is to

BRIEF SUMMARY

Current Knowledge/Study Rationale: The purpose of this study was to investigate the relationship between CPAP adherence and sustained attention in patients with moderate to severe OSA. Based on findings of previous studies, we predicted that an objective assessment of attention (Psychomotor Vigilance Task) would detect attention-related improvements in behavior resulting from CPAP therapy.

Study Impact: The results of this study show that the more that CPAP therapy is used, the better the patient outcome as measured by the PVT. This finding is of importance because it emphasizes the importance of treatment adherence on a performance-based sleep outcome measure.

focus on the assessment of attention. The Psychomotor Vigilance Task (PVT) is a sustained attention and reaction time test that has seen widespread use in the study of sleep and circadian rhythms.[25–28] It has been demonstrated to be sensitive to deficits in alertness and sustained attention, both of which are commonly observed in patients with OSA,[24] as well as improvements in these domains resulting from treatment.[29–32] A number of studies have provided evidence that attention-related impairments resulting from OSA can significantly improve following treatment with CPAP.[33–36] The PVT may be a useful addition to subjective self-reported assessments already used by sleep providers because it is an objective measure of alertness and attention.

The two most heavily studied PVT metrics are minor lapses of attention and reaction time. Although reaction time is the most direct measure of attention, studies that have used the PVT in the field of sleep medicine have found that minor lapses are most associated with impairments in vigilance.[37,38] Of particular interest are findings from operational research that show PVT minor lapses were found to be very informative in assessments of fatigue-related performance deficits in real-world settings.[39,40]

Few studies have explored the relationship between CPAP treatment adherence and objective measures of alertness and attention in patients with OSA in clinical contexts. The goal of this study was to investigate the relationship between CPAP adherence and an objective measure of alertness and attention.

METHODS

Participants

Two hundred forty participants were recruited from the pulmonary sleep clinic at the Veterans Affairs San Diego Healthcare System. Inclusion criteria were as follows: patients with a new diagnosis of moderate to severe OSA (AHI > 15 events/h)[41] for whom CPAP therapy had been prescribed. The pulmonary sleep clinic primarily utilizes home sleep apnea tests for diagnosis (Stardust II, Respironics, Murrysville, Pennsylvania, United States). Patients who resided outside of San Diego county, were not English-speaking, had visual impairments preventing assessment with the PVT, had significant cognitive impairment, who could not commit to completing the study, or who had fatal comorbidities (life expectancy < 6 months as indicated by treating physician) were considered for study exclusion.

All participants provided written informed consent in accordance with University of California San Diego Human Research Protection Program guidelines. Each participant completed a series of standardized sleep-related questionnaires at baseline and 6-month visits. The PVT was administered via handheld device at baseline and subsequent follow-up visit. CPAP adherence was determined from unit usage data. These data allowed hours of machine use per night at prescribed pressure (CPAP adherence) to be objectively determined. Participants in the self-management care (SMC) group were provided with supplementary group instruction about OSA and CPAP treatment at their baseline visit, whereas participants in the usual care (UC) group received routine clinical education and support. All participants received monetary compensation for participation in the study.

Apparatus

Continuous Positive Airway Pressure Equipment

Participants were provided with REMstar Pro (Respironics, Pittsburgh, Pennsylvania, United States) flow generators. All participants were allowed to choose between a variety of masks (full-face, nasal, or pillow), and were given the opportunity to familiarize themselves with their CPAP unit prior to beginning the study. Pressure determination was accomplished via algorithm.[42] Each unit was equipped with a secure digital card that stored adherence and efficacy data. Data were downloaded using manufacturer software at follow-up visits in order to measure treatment adherence, which was defined as the amount of time that the mask was worn at the prescribed pressure level over the defined period of time, and is reported in h/night.

Psychomotor Vigilance Task

The PVT is an objective measure of vigilance performance[43] and has been demonstrated to be sensitive to sleep loss and recovery regardless of cause.[44,45] For OSA, there is not good evidence of a clear dose-response relationship between the primary measure of sleep apnea severity (ie, AHI) and PVT as one might expect,[24,28,29] with the likely reason being that AHI is not highly correlated with daytime symptoms and functioning. However, measures of daytime sleepiness are related to the PVT in patients with OSA.[24,29] The original PVT validation was based on a 10-minute PVT task,[43] but more recently the 7-minute PVT,[46] 5-minute,[26] and 3-minute versions have all been validated.[47,48]

The Walter Reed version of the PVT was utilized for the study and is a visual task.[46] The PVT was administered to participants using a handheld device during normal business hours, typically between 8:00 AM and 4:00 PM. Each session consisted of 100 visual presentations of a target stimulus for 50 milliseconds, with random interstimulus intervals ranging from 3 to 7 seconds. Participants were instructed to respond to target stimuli with their dominant hand by tapping the screen as quickly and accurately as possible. The total duration of each PVT session was 7 minutes. Two PVT metrics were utilized for the study: reaction time and minor lapses of attention. Reaction time was defined as the amount of time between stimulus presentation and participant response. A minor lapse of attention was defined as a failure to respond to a target stimulus in less than 500 milliseconds.

Questionnaires

Participants completed questionnaires at baseline and subsequent follow-up visits. Demographic information collected at baseline included age, sex, education, marital status, height, and weight. Patient-reported assessments of daytime sleepiness and sleep quality were obtained using the Epworth Sleepiness Scale[49,50] and Pittsburgh Sleep Quality Index, respectively.[51] Baseline comorbidity was assessed using the Charlson Comorbidity Index.[52]

Data Analysis

Descriptive statistics were used to summarize baseline characteristics, CPAP adherence, and PVT parameters. All continuous variables are reported in mean ± standard deviation and range. Data analyses were performed using R version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria).

Outcome measures were PVT metric change (number of minor lapses and reaction time) and were calculated by subtracting the PVT metric of interest at baseline from corresponding metric after 6 months of treatment with CPAP. Participants who completed both baseline and 6-month assessments were included in the analysis. To account for any missing data from baseline to 6-month assessment, we examined the difference in the baseline variables between patients with complete data and patients with missing 6-month assessment data using Wilcoxon rank test and Fisher exact test. Although we found that there were marginally significant differences in age between these two groups of patients, other covariates were not significantly different.

Simple and multiple linear regression analyses were performed to examine the association between the PVT parameters (change in mean reaction time, change in minor lapses of attention) and CPAP adherence at the 6-month time point. Study group, baseline age, baseline body mass index, baseline comorbidity, baseline AHI, and baseline PVT metrics were considered as covariates in the multiple regression model. Backward elimination was used to remove insignificant variables from the model and the variable with the largest P value was removed from the model at each step. Variables with values of $P < .10$ were kept in the final main model and CPAP adherence was retained in the model regardless of its significance level because it was the primary variable of interest in our study. A normal probability plot was used to assess the normality assumption of model residuals and influential observations were assessed by residual and Cook distance. Potential interaction between CPAP adherence and study group was also assessed by adding an interaction term into the final main effect model. Sensitivity analyses were performed by excluding the influential observations from the analysis and comparing to the original model. We define statistical significance as $P < .05$ and marginal statistical significance as $P < .10$.

RESULTS

Sample Characteristics

The final study sample included 114 participants who completed both baseline and 6-month visits. We assessed the difference in baseline covariates (age, AHI, body mass index, Epworth Sleepiness Scale score, Pittsburgh Sleep Quality Index total score, comorbidity, reaction time, and number of minor lapses and study group assignment) between patients with complete data and patients with missing 6-month assessment data and we found that although age difference was marginally significant between the 2 groups of patients (57.5 ± 11.6 for participants with 6-month assessment versus 54.7 ± 13.2 for participants without 6-month assessment, $P = .035$), other baseline covariates did not significantly differ.

Table 1—Sample characteristics (n = 114).

Baseline	
Sex (% male)	96.5%
Age (years)	57.5 ± 11.6 (28 to 84)
AHI (events/h)	37.8 ± 20.0 (14.6 to 112)
Body mass index (kg/m^2)	33.9 ± 6.25 (19 to 63)
ESS score	12.6 ± 5.6 (2 to 22)
Pittsburgh Sleep Quality Index	11.1 ± 3.0 (5 to 18)
PVT RT (milliseconds)	419 ± 201 (212 to 1296)
PVT minor lapses	11.2 ± 15.7 (0 to 60)
Month 6	
Sex (% male)	96.4%
Change in ESS score	−5.39 ± 5.48 (−18 to 6)
CPAP adherence (hours)	3.32 ± 2.53 (0 to 9.29)
PVT RT (milliseconds)	346 ± 179 (206 to 1524)
PVT minor lapses	6.39 ± 11.0 (0 to 56)
Change in PVT RT (milliseconds)	−73.1 ± 211 (−950 to −831)
Change in PVT minor lapses	−4.77 ± 13.2 (−55 to 21)

Values presented as mean ± standard deviation (range) unless otherwise indicated. AHI = apnea-hypopnea index, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, PVT = Psychomotor Vigilance Task, RT = reaction time.

Table 1 contains baseline demographic information for study participants. At baseline, the sample had an average age of 57.5 ± 11.6 and an average AHI of 37.8 ± 20.0 events/h of sleep. A total of 96.5% of the sample was male at baseline and 96.4% at month 6. At baseline, average mean PVT reaction time was 419 ± 201 milliseconds, and baseline average number of minor lapses of attention were 11.2 ± 15.7. Average CPAP adherence over 6 months was 3.32 ± 2.53 hours. Compared to baseline PVT measures, the average number of minor lapses at month 6 were reduced by 4.77 and the average reaction time at month 6 was reduced by 73.1 milliseconds.

Linear Regression Analyses

Simple linear regression analysis did not show any significant association of CPAP adherence with either change in mean reaction time or change in mean number of minor lapses. However, after adjusting for potential covariates, CPAP adherence was significantly associated with a change in the number of minor lapses ($\beta = -0.72$, standard error [SE] = 0.34, $P = .037$), such that more hours of CPAP use was associated with greater reduction in the mean number of minor lapses (**Table 2**). Higher baseline minor lapses were associated with a greater reduction in minor lapses at 6 months ($\beta = -0.65$, SE = 0.05, $P < .0001$) and participants in the self-management care group had greater reduction in minor lapses than participants in the UC group ($\beta = -4.35$, SE = 1.65, $P = .010$). We did not see a substantial change in the results of the sensitivity analyses when three influential observations were excluded. The interaction between study group and CPAP adherence was also significantly ($P = .032$) associated with change of minor lapses, but became nonsignificant while excluding three influential observations ($P = .22$).

Table 2—Multiple linear regression (n = 114).

	Change in Minor Lapses at 6 mo			Change in Reaction Time at 6 mo		
	β	SE	*P*	β	SE	*P*
6 mo CPAP adherence (h/night)	−0.72	0.34	.037	−10.50	6.19	.092
Group (SMC versus UC)	−4.35	1.65	.010	−83.40	30.00	.006
Baseline RT (milliseconds)	–	–	–	−0.69	0.08	< .001
Baseline minor lapses	−0.65	0.05	< .001	–	–	–

Baseline age and baseline apnea-hypopnea index were not significant and therefore not included in the final model. CPAP = continuous positive airway pressure, RT = reaction time, SE = standard error, SMC = self-management care, UC = usual care.

For change in mean reaction time, we also found that higher CPAP adherence was associated with a greater reduction in mean reaction time (β = −10.5, SE = 6.19, *P* = .092, marginally significant). This association became nonsignificant (β = −5.16, SE = 3.69, *P* = .17) in the sensitivity analysis after excluding three influential observations; however, the direction of the association remained the same. The interaction between study group and CPAP adherence was marginally significant (*P* = .06) and associated with change of reaction time, but became highly nonsignificant while excluding three influential observations (*P* = .43).

DISCUSSION

Our results suggest that CPAP adherence is associated with significant improvements in vigilance after 6 months of treatment with CPAP. Minor lapses have been shown to be one of the best PVT metrics in terms of their relationship to operational functioning during the day.[39] Of note, participants in the SMC group were simply provided with extra education and support about sleep apnea and CPAP therapy; the intervention did not change pressure levels and was only considered a supplement to routine clinical education and support. However, the data showed that participants in the SMC group had a greater reduction in minor lapses than those in the UC group. Overall, the number of minor lapses were nearly cut in half. Based on an operational PVT publication that used a cutoff of 11 minor lapses as a threshold for cognitive impairment, the level of CPAP adherence studied in our sample, while modest at under 4 h/night, still resulted in a normalization of the number of minor lapses.[39] Our data support the hypothesis that CPAP adherence is associated with attentional improvements in patients with moderate to severe OSA.

Few studies have directly examined the relationship between CPAP adherence and PVT metrics. One early study with a small sample size (n = 12) found a significant relationship between a measure of reaction time and CPAP adherence such that those participants who were deemed "compliant" had a significant drop in reaction time relative to those deemed "noncompliant."[34] Another study that examined a larger CPAP adherence intervention trial (n = 250) did not find a relationship between CPAP adherence and PVT despite finding significant relationships for reduction of sleep symptoms, depressive symptoms, and improvement in functional outcomes.[53] One plausible explanation for the negative finding in this study was the low adherence rate (median adherence in intervention group = 2.4 h/night; control group = 1.5 h/night). The findings of the current study extends these findings by providing a multivariate regression analysis that takes into account important covariates and includes both a higher mean rate of adherence and range of adherence (from 0 to 9.2 h/night).

One previous report on the "response shift" in pretherapy patients with sleep apnea (relative to their subjective reporting after staring therapy) underscores the difficulty many patients with sleep apnea have in accurately reporting their daytime sleepiness levels and other subjective measures as well.[54] Our findings provide additional support for the use of the PVT as a practical screening and assessment tool for patients with OSA that is sensitive to both attention-related deficits of OSA and attentional improvements resulting from CPAP treatment.[47,55]

There are some limitations of this study. Other objective measures of sleepiness were not used as comparators, such as the Multiple Sleep Latency Test. The sample was primarily male. Due to the sample composition, analyses were limited to patients with AHI ≥ 15 events/h. Finally, the timing of PVT administration was not recorded and therefore any effect of time of day on vigilance could not be examined in this study. Several studies seem to indicate little effect of circadian phase on PVT in participants with normal sleep-wake schedules.[56–58] To allow for a more detailed assessment of the relationship between CPAP adherence and vigilance, future research would benefit from the inclusion of additional objective measures of daytime sleepiness such as the Multiple Sleep Latency Test, a broader sample demographic, patients with a wider range of OSA severity (ie, inclusive of mild OSA), and analysis of a possible circadian effect on vigilance.

ABBREVIATIONS

AHI, apnea-hypopnea index
CPAP, continuous positive airway pressure
ESS, Epworth Sleepiness Scale
OSA, obstructive sleep apnea
PVT, Psychomotor Vigilance Task
SD, standard deviation
SE, standard error
SMC, self-management care
UC, usual care

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