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Effect of 3 weeks of continuous positive airway pressure treatment on mood in patients with obstructive sleep apnoea: a randomized placebo-controlled study

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Abstract

Background—Patients with obstructive sleep apnoea (OSA) commonly have mood symptoms such as depression and anxiety. However, the results of randomized controlled trials on the therapeutic effect of CPAP on mood symptoms have been inconsistent. The present study examined whether 3 weeks of CPAP treatment had specific therapeutic effects on mood symptoms in patients with OSA compared with placebo.

Methods—A double-blind, parallel, randomized controlled trial using therapeutic and placebo CPAP was performed in 71 patients newly diagnosed with OSA [apnoea-hypopnoea index (AHI) ≥ 10]. Mood was assessed by the Center for Epidemiologic Studies-Depression (CES-D) Scale, the Profile of Mood States (POMS) and the Brief Symptom Inventory (BSI) before and after 3 weeks of treatment. AHI was used to assess the severity of apnoea. The two groups were compared using a simple comparison of the changes within each arm and repeated measures analysis of variance.

Results—Fifty-six subjects completed the study: 26 in the CPAP group and 30 in the placebo group. The two groups were well matched at baseline, with no significant differences in demographic, mood and apnoea variables. Both groups had severe apnoea, and mild depression and anxiety at baseline. After 3 weeks of treatment, AHI decreased significantly in the CPAP group. The mean change in AHI was -30.7 [standard deviation (SD) 23.1] in the CPAP group and -5.8 (SD 18.3) in the placebo group (difference between groups $P < 0.001$). However, after 3 weeks of treatment, there were no significant time by treatment effects in relation to mood, as assessed by the CES-D, POMS Depression, POMS Tension, BSI Depression or BSI Anxiety (all $P > 0.05$).

Conclusion—In conclusion, 3 weeks of CPAP treatment did not show a specific therapeutic effect on mood symptoms in patients with OSA.

Keywords

Obstructive sleep apnoea; CPAP; Mood; Depression; Anxiety; Double-blind placebo-controlled

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Conflict of interest statement

None declared.

1. Introduction

Obstructive sleep apnoea (OSA) is a chronic condition characterized by repetitive upper airway obstruction during sleep, leading to hypoxaemia and recurrent arousals from sleep [1]. It has been estimated that 2-4% of middle-aged men and 1-2% of middle-aged women suffer from OSA [2].

OSA is associated with daytime sleepiness, impaired cognition and quality of life, and cardiovascular morbidity. Patients with OSA can also have increased depression and anxiety symptoms [3]. There is increasing research interest in the mood in patients with OSA [4]. However, the exact relationship between the severity of OSA and mood symptoms is still not certain.

Numerous studies have been conducted to determine whether OSA treatment affects mood symptoms. Interestingly, while many uncontrolled studies have reported that continuous positive airway pressure (CPAP) treatment improves mood symptoms [5-7], the results of randomized controlled trials of the therapeutic effect of CPAP on mood symptoms have been inconsistent. Table 1 summarizes the findings of randomized placebo-controlled trials which have evaluated the effect of CPAP treatment on mood in patients with OSA. Some studies did not find any significant difference between CPAP and placebo groups [8-11], while other studies reported that CPAP treatment lowered depression and anxiety symptoms in patients with OSA [3,12-16].

Previously, in two separate cohorts, the authors found no specific treatment effects on mood after 1 week of CPAP vs subtherapeutic CPAP treatment, or 2 weeks of active CPAP vs sham CPAP treatment [10,16]. However, CPAP treatment was found to have a consistent positive effect on fatigue [17]. The present study examined the latter cohort of patients to determine if a longer period of CPAP treatment (i.e. 3 weeks) would show a beneficial effect on depression and anxiety compared with placebo.

2. Methods

2.1. Participants

Seventy-one CPAP-naïve men and women with OSA were studied as part of a randomized double-blind clinical trial comparing 3 weeks of CPAP treatment with placebo. Subjects were recruited by advertisements and word-of-mouth referral in the San Diego area. Subjects were excluded if they reported a history of major medical illnesses (other than OSA and hypertension), had a current psychiatric diagnosis, were receiving psychotropic or sedative hypnotic medication, were pregnant, or had ever received treatment for OSA. Subjects who were receiving antihypertensive medications ($n=2$) had their medications slowly tapered and participated after a 3-week washout period. The protocol was approved by the University of California San Diego (UCSD) Human Subjects Institutional Review Board in 2004 (Approval Number 041411), and all subjects provided written informed consent. Patients were recruited between 2004 and 2009. Study recruitment is shown in Fig. 1.

2.2. Procedure

Initial OSA screening was conducted with an unattended home sleep study (Stardust II Home Monitoring System, Respiromics Inc.). Subjects with an apnoea-hypopnoea index (AHI) ≥ 10 were given a provisional diagnosis of OSA and were admitted to the UCSD General Clinical Research Center Gillin Laboratory of Sleep and Chronobiology (GCRC-GLSC) at 17:00 h for assessment. On the first night at the GCRC-GLSC, sleep was monitored by polysomnography from 22:00 to 6:00 h the next morning. Those subjects who

still had AHI ≥ 10 were diagnosed with OSA and randomized in a 1:1 allocation ratio to receive either CPAP or placebo in a double-blind fashion. A permuted block design was used with a block size of 10. The randomization list was generated by the study statistician. Participants, the principal investigator and the staff responsible for obtaining study outcomes were blinded to the treatment assignment.

Subjects returned to the GCRC-GLSC the following night for CPAP titration. Those randomized to the CPAP group underwent standard CPAP titration. CPAP treatment was started at a pressure of 4 cmH₂O, and was increased by 1-2-cmH₂O increments based on the presence of apnoeas, hypopnoeas, snoring or respiratory-effort-related arousals. Titration was considered successful when all significant respiratory events stopped and the patient had spent at least 15 min asleep in the final CPAP level. Subjects randomized to the placebo group underwent a mock titration night.

Subjects continued their treatment (CPAP or placebo) at home for 3 weeks. Proper use and set-up of equipment was monitored by scheduled telephone calls and home visits by a sleep technician who was not involved in the outcome assessments. Subjects received frequent reminders to comply with treatment, and usage (h/day) was logged on the CPAP machine and analysed at the end of the treatment period. After 3 weeks of treatment, subjects returned to the GCRC-GLSC for further assessment.

2.3. Polysomnography

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 piezo-electric belts. Finger pulse oximetry was used to measure average oxygen saturation. Sleep records were scored manually according to the criteria of Rechtschaffen and Kales [18]. Sleep efficiency, defined as the total sleep time divided by the total time in bed, was computed. Apnoeas were defined as decrements in airflow of $\geq 90\%$ from baseline for ≥ 10 s. Hypopnoeas were defined as decrements in airflow of $\geq 50\%$ but $< 90\%$ from baseline for ≥ 10 s regardless of the presence or absence of significant desaturations ($\geq 3\%$) or micro-arousals. The numbers of apnoeas and hypopnoeas per hour were calculated to obtain AHI. Subjects with AHI ≥ 10 were considered to have OSA and were admitted to the study.

2.4. CPAP

The same CPAP system was used in both groups (ResMed S7 Elite CPAP with HumidAire 2i™ Integrated Heated Humidifier; ResMed Corp., San Diego, CA, USA). On the first night, the appropriate CPAP mask (therapeutic or placebo) was fitted and the patient was trained in the use of the equipment.

2.5. Placebo

The placebo system was a modified version of the sham CPAP reported by Farre et al. [19]. In the present study, placebo consisted of a modified nasal or full face (naso-oral) CPAP mask with ten 1/4-inch drill holes to allow free exchange of air during inhalation and exhalation, plus a pressure reducer placed in the CPAP tubing. With this system, the CPAP generator could be placed at any pressure to control for machine noise, but the pressure at the nose and mouth was 0.5 cmH₂O during exhalation and 0 cmH₂O during inhalation. Of importance to the placebo blinding, the subject was able to feel a gentle breeze at the nose. The pressure was set at 8 cm H₂O to control for CPAP blower noise.

2.6. Psychological assessment

2.6.1. Primary outcome measures—The Profile of Mood States (POMS) Depression scale was used as the primary outcome for the study power calculations because data from a previous study [16] showed a non-specific effect of 1 week of CPAP treatment on this mood variable. It was hypothesized that 3 weeks of treatment would result in a similar sustained decrease in subjective mood complaints for the CPAP group, and that changes in mood scores would be transient and would not be evident at 3 weeks in the placebo group.

2.6.2. Secondary outcome measures—To determine if there was convergent validity in the findings, multiple measures of depression [Center for Epidemiologic Studies-Depression (CES-D), Brief Symptom Inventory (BSI) Depression] and anxiety (POMS Tension, BSI Anxiety) were employed

All subjects completed a psychological assessment at baseline and after 3 weeks of treatment.

The POMS is a well-established, factor-analytically derived measure of psychological distress with high levels of reliability and validity [20]. It consists of 65 adjectives rated on a five-point scale (0 = not at all to 4 = extremely) that can be consolidated into six subscales. The POMS total score and subscales have been used in a variety of chronically ill and healthy populations, including patients with OSA [16]. The POMS Depression and Tension subscales were used in this study.

The CES-D scale is a 20-item self-report scale that has been shown to be reliable and valid for the assessment of depressive symptoms [21]. CES-D scores ≥ 16 are considered to indicate depressed mood. The CES-D primarily taps cognitive/affective aspects of depression, and has been shown to be useful in chronically ill groups, including patients with OSA.

The BSI was derived from the Symptom Check List-90-revised and has been used extensively in diverse populations as a screening instrument for global psychological distress. The BSI is a 53-item self-administrated questionnaire that uses five-point Likert scales and yields nine dimensions: somatization, obsessive-compulsive, depression, anxiety, interpersonal sensitivity, hostility, phobic anxiety, paranoid ideation and psychoticism [22].

2.7. Data analyses

Student's *t*-test, Chi-squared test and Fisher's exact test were used to compare the means of demographic variables, depression and anxiety scores, AHI and average oxygen saturation between the two groups at baseline.

Differences between the CPAP and placebo groups (using the change from baseline as the outcome variable) were assessed with an independent sample *t*-test. Differences between and within the two groups over time were assessed using repeated measures analysis of variance for the raw mood variable scores. This analysis allowed testing for the main effects of treatment (CPAP vs placebo), time (baseline vs post-treatment) and time by treatment. A time effect alone would imply that the treatment itself had no specific effect on the variable of interest (i.e. a placebo effect). On the other hand, a treatment by time effect would imply that one of the treatment groups responded to treatment over time differently than the other treatment group.

Using self-reported mood data in patients with OSA from a previous protocol, a calculation was performed to assess minimum mood change, assuming an α error of 5% and statistical power of 80%. The resulting sample size was 40 patients in each group.

Data were analysed using Statistical Package for the Social Sciences Version 17.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $P < 0.05$.

3. Results

3.1. Sample characteristics

Nine women and 47 men completed the study. Three subjects experienced skin irritation due to the CPAP mask (one completed the study and two dropped out). The sample characteristics are presented in Table 2. There were no significant differences in age, body mass index, depression, anxiety or severity of apnoea between the groups at baseline.

3.2. Treatment effects on sleep

After 3 weeks of treatment, AHI decreased significantly in the CPAP group, and the change from baseline was significantly higher compared with that observed in the placebo group. There were no significant differences in changes from baseline between the two groups for average oxygen saturation, sleep efficiency or minimum oxygen saturation (Table 3).

3.3. Treatment effects on mood

There were no significant changes in the CES-D, POMS Depression, POMS Tension, BSI Depression or BSI Anxiety scores in either group after 3 weeks of treatment ($P > 0.1$) (Table 3). Table 4 shows mean baseline and post-treatment scores for the mood variables in the two groups. No significant time effects or time by treatment effects were found for the CES-D, POMS Depression, POMS Tension or BSI Depression scales. However, a significant time effect (but no time by treatment effect) was observed for the BSI Anxiety scale.

4. Discussion

Few studies have examined the effects of CPAP treatment on mood using controlled clinical trial methodology (Table 1), and the literature is quite inconsistent. However, a review found that CPAP was associated with a positive effect on mood symptoms in five crossover studies. These studies employed CPAP trials lasting 3-4 weeks [23]. In the present study, while CPAP had the expected beneficial and specific effect on the severity of apnoea, there were no significant improvements in any depression or anxiety measures. The results replicate the authors' previous findings in different patient and treatment cohorts [10,16]. Taken as a whole, these findings call into question the effects of CPAP on anxiety and depression, and suggest the need for further blinded studies.

The BSI Anxiety scale improved significantly over time, but did so equally for both groups. Interestingly, and consistent with the authors' previous results, an intervention consisting of a caring physician and believable but not functioning CPAP had a significant independent beneficial effect on patients' anxiety symptoms.

One limitation of this study was that it did not meet one of the CONSORT guidelines, as it was never formally registered as a randomized clinical trial. Future clinical trials in this area should satisfy the CONSORT guidelines.

Five suppositions are discussed below to see whether the limitations of the study's design might account for the lack of effect of CPAP on mood.

Firstly, although CPAP did not show superiority to placebo in terms of effect on mood, these observations may reflect the relatively low severity of disruptive mood symptoms at baseline. For instance, only 35% and 20% of subjects in the CPAP and placebo groups, respectively, showed high baseline levels of depression (i.e. CES-D ≥ 16). Given the low

prevalence of symptoms at baseline, there could be a 'floor effect' which could have contributed to the negative finding. To investigate this, a secondary analysis was performed to examine if CPAP would be effective on the patients whose depression scores were above threshold (i.e. CES-D ≥ 16). There were 15 such individuals (nine in the CPAP group and six in the placebo group). Their CES-D scores were not significantly different at baseline (mean 22.4 vs 21.8 for the CPAP and placebo groups, respectively; $P=0.430$). In these individuals, there was a trend for a time effect ($P=0.063$); depression levels improved, on average, by 14%. However, there was no significant time by treatment effect ($P=1.000$). Obviously, the sample size is limited for analysis based on categorical diagnosis of depression but, in the current sample, there was no suggestion that CPAP had a specific effect on ameliorating the symptoms of major depression.

Secondly, exploratory analysis was undertaken to determine if adherence to treatment was related to improvements in mood symptoms. Average compliance, measured in h/day, was examined in terms of changes in mood from baseline to post-treatment. There was no suggestion that treatment compliance affected change in mood ($P=0.301$). It should be noted that, overall, the sample had good compliance. It is possible that in a routine clinic setting where compliance can be very problematic, the relationship between CPAP compliance and mood change could be significant and would need to be considered in terms of studying the effects of CPAP treatment on mood.

Thirdly, was the length of the clinical trial sufficient to reveal an effect on mood? Three weeks of treatment might not be sufficient and a longer trial may be required to demonstrate specific beneficial effects of CPAP treatment on mood. Nonetheless, it has previously been shown that, at least for fatigue symptoms, 3 weeks of CPAP treatment has a readily discernable effect [17].

Fourthly, could the null findings reflect limited power? There are a number of ways to consider this important question. (1) Table 1 summarizes the existing double-blind literature in this area; the sample size for the present study was similar to that reported for other studies. (2) Not even a trend (i.e. $P<0.1$) for a time by treatment effect was found in this study (Table 4); thus, it is unlikely that the non-significant findings would have proven to be significant if a larger sample size had been used. (3) The effect sizes for the intervention effects of CPAP treatment on the five mood variables were universally small: -0.089 (CES-D), 0.014 (POMS Depression), -0.147 (POMS Tension), -0.146 (BSI Depression) and -0.237 (BSI Anxiety). The study randomized 71 patients with OSA to CPAP treatment ($n=34$) or placebo ($n=37$), and had 80% power to detect a treatment difference effect size of 0.68 (two-sided $\alpha=0.05$) if all of the subjects completed treatment. The current analysis is based on 56 subjects who had complete data for the mood variables at both visits, and has 80% power to detect a treatment effect size of 0.77. (4). It is possible that basing an analysis on completers could bias the results. The dropout rate was not significantly different between the placebo group (16.7%) and the CPAP group (25.7%) ($P=0.396$, Fisher's exact test). However, the non-completers had significantly higher AHI scores but were indistinguishable from the completers in terms of key covariates such as demographic and mood variables. Given the null treatment effects observed in this analysis on completers, it is unlikely that a more conservative intent-to-treat analysis would qualitatively change the results. More importantly, the detection of effect sizes between 0.15 and 0.24 would require considerably larger sample sizes, ranging from 275 to 700 participants per group ($\alpha=0.05$), to detect these putative small effects of 3 weeks of CPAP treatment on mood. On the other hand, a larger sample size would facilitate the examination of subgroups of patients with OSA whose mood symptoms might be more responsive to CPAP treatment.

Finally, it is possible that future trials should enrol patients with more sleep disturbances and psychiatric or medical morbidities in order to exclude a floor effect. The present sample excluded patients with major medical illnesses other than OSA and hypertension. However, these exclusion criteria could serve to limit some important confounders that could affect mood symptoms in typical OSA patients with medical comorbidities. It is possible that CPAP treatment may be more helpful to patients with medical comorbidities such as diabetes.

The importance of blinded clinical trials in determining the efficacy of CPAP on mood symptoms has been recognized and supported by many researchers, and recently by National Institute of Health initiatives. However, in the past 10 years, there has been very little progress in this area, and only one new paper [24] has been published since the present authors conducted a 2-week randomized placebo-controlled study of mood in 2007 [10].

In conclusion, although it is clear that CPAP treatment improves respiratory disturbances, 3 weeks of CPAP treatment did not show a specific therapeutic effect on mood symptoms in patients with OSA. Double-blind placebo trials in subjects with OSA with a higher level of mood symptoms may be necessary to establish the specific treatment benefits of CPAP on mood symptoms.

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Fig. 1.
Recruitment profile. CPAP, continuous positive airway pressure.

Table 1

Studies evaluating the efficacy and/or effectiveness of continuous positive airway pressure (CPAP) treatment compared with oral placebo, sham CPAP treatment, conservative treatment and oral appliance on mood in patients with obstructive sleep apnoea (OSA).

Reference	Year	Subject characteristics	Type and duration of the treatment (mean compliance time in parentheses)	Key findings
Engleman et al. [14]	1994	32 subjects (AHI=28) [crossover design; 16 began with CPAP, 16 with placebo]	CPAP (3.4 h) compared with oral placebo over 4 weeks	Improvement in mood (POMS) with CPAP ($P<0.05$)
Engleman et al. [15]	1997	16 subjects (AHI in the range 5–14.9 + two or more symptoms of SAHS) [crossover design; eight began with CPAP, eight with placebo]	CPAP (2.8 h) compared with oral placebo over 4 weeks	Significant improvement in depression (HADS) with CPAP ($P=0.03$)
Engleman et al. [9]	1998	23 subjects (≥ 15 apnoeas + hypopnoeas + symptoms of OSA) (AHI=43) [crossover design; 13 began with placebo, 10 with CPAP]	CPAP (2.8 h) compared with oral placebo over 4 weeks	No differences in anxiety or depression (HADS) between CPAP and oral placebo
Engleman et al. [13]	1999	34 subjects [AHI in the range 5–15 + two symptoms of SAHS (ESS ≥ 8 or sleepiness while driving)] [crossover design; 17 began with CPAP, 17 with placebo]	CPAP (2.8 h) compared with oral placebo over 4 weeks	Significantly lower depression but not anxiety (HADS) after CPAP ($P<0.01$)
Yu et al. [16]	1999	Group 1=20 subjects (RDI=45.9); group 2=14 subjects (RDI=35.2)	CPAP (5.6 h) compared with sham CPAP (5.2 h) over 1 week	Significant improvement in mood in both groups (all POMS subscales except POMS Vigor)
Barnes et al. [8]	2002	42 subjects (AHI=12.9)	CPAP (3.53 h) compared with oral placebo over 8 weeks	No significant differences between CPAP and oral placebo on mood (POMS, BDI)
Barnes et al. [3]	2004	Three-phase crossover design ($n=99$) (AHI=21.5)	CPAP (3.6 h) compared with an MAS (5.5 h)	CPAP improved general mood (POMS) and depression
			and a placebo tablet over 3 months	compared with an MAS (improvement only in POMS Tension-Anxiety subscale). The BDI responded equally to all three treatments
Marshall et al. [11]	2005	Mild OSA patients ($n=29$) CPAP group (AHI=21) Placebo group (AHI=22)	Randomized controlled crossover trial (3 weeks of CPAP or sham CPAP treatment)	Mood (HADS) was not improved more than sham CPAP
Haensel et al. [10]	2007	CPAP treatment group ($n=25$, AHI=64) Placebo CPAP group ($n=25$, AHI=58)	CPAP (6.6 h) and placebo CPAP (6.0 h) over 2 weeks	No specific beneficial impact of CPAP treatment on mood in patients with OSA

Reference	Year	Subject characteristics	Type and duration of the treatment (mean compliance time in parentheses)	Key findings
Cooke et al. [24]	2009	OSA patients with mild-to-moderate Alzheimer's disease ($n=10$)	Sustained-CPAP-use group (13 months) compared with no-CPAP-use group	Sustained-CPAP-use group's depressive symptoms (based on CSD) showed less deterioration compared with the no-CPAP-use group

AHI, apnoea-hypopnoea index; SAHS, sleep apnoea/hypopnoea syndrome; HADS, Hospital Anxiety and Depression Scale; BDI, Beck Depression Inventory; HADS, Hospital Anxiety and Depression Scale; POMS, Profile of Mood States; RDI, Respiratory Disturbance Index; MAS, mandibular advancement splint; CSD, Cornell Scale for Depression.

Table 2

Baseline demographic and sleep data in total subjects.

		CPAP (n=26)	Placebo (n=30)
Age, years		48.3 (9.9)	48.2 (9.0)
Body mass index, kg/m ²		29.8 (4.6)	28.6 (3.8)
Gender	Male	22	25
	Female	4	5
Race/ ethnicity	White	23	24
	Black	3	4
	Asian	0	1
	Other	0	1
CES-D		12.5 (8.6)	9.6 (6.8)
POMS Depression		7.3 (7.8)	6.7 (8.8)
POMS Tension		7.6 (4.5)	6.4 (5.8)
BSI Depression		0.5 (0.5)	0.3 (0.4)
BSI Anxiety		0.5 (0.4)	0.3 (0.4)
Apnoea–hypopnoea index (events/h)		36.7 (21.8)	31.3 (18.6)
Average oxygen saturation (%)		94.7 (1.9)	95.3 (2.0)
Minimum oxygen saturation (%)		79.8 (10.3)	80.7 (12.5)

CPAP, continuous positive airway pressure; CES-D, Center for Epidemiologic Studies Depression Scale; POMS, Profile of Mood States; BSI, Brief Symptom Inventory.

Data given as mean (standard deviation).

Table 3

Mean (standard deviation) changes from baseline in patients randomized to continuous positive airway pressure (CPAP) treatment and placebo.

	CPAP (n=26)	Placebo (n=30)	95% CI of the difference	P-value
Apnoea-hypopnoea index	-30.7 (23.1) ^a	-5.8 (18.3) ^b	13.7–36.3	<0.001
Average O ₂ saturation (%)	0.7 (4.5) ^a	0.1 (2.1)	-2.5–1.3	0.536
Sleep efficiency	0.5 (9.7) ^a	-0.3 (7.8) ^b	-5.6–4.0	0.745
Minimum O ₂ saturation (%)	7.9 (10.7) ^a	1.4 (18.2) ^b	-14.9–1.8	0.121
CES-D	0.3 (7.0) ^c	0.9 (6.9)	-3.2–4.4	0.748
POMS Depression	-1.1 (6.0)	-1.2 (6.9)	-3.6–3.4	0.959
POMS Tension	-1.4 (4.6)	-0.7 (4.7)	-1.8–3.2	0.585
BSI Depression	-0.4 (0.4)	0.0 (0.3) ^b	-0.1–0.2	0.591
BSI Anxiety	-0.1 (0.3)	-0.1 (0.3) ^b	-0.1–0.3	0.383

AHI, apnoea-hypopnoea index; CES-D, Center for Epidemiologic Studies Depression Scale; POMS, Profile of Mood States; BSI, Brief Symptom Inventory; CI, confidence interval.

^a n=25.

^b n=29.

^c n=24.

Mean and standard deviations of mood variables before and after 3 weeks of continuous positive airway pressure (CPAP) treatment.

Table 4

Neuropsychological test	Placebo (n=30)		CPAP (n=26)		P-value	
	Day 1	Day 21	Day 1	Day 21	Time	× Treatment
CES-D ^a	9.6 (6.8)	10.5 (7.6)	12.5 (8.8)	12.7 (9.9)	0.561	0.748
POMS Depression	6.7 (8.8)	5.6 (6.9)	7.3 (7.8)	6.2 (7.2)	0.202	0.959
POMS Tension	6.4 (5.8)	5.7 (4.9)	7.6 (4.5)	6.2 (6.0)	1.000	0.585
BSI Depression ^b	0.3 (0.4)	0.3 (0.4)	0.5 (0.5)	0.5 (0.5)	0.759	0.591
BSI Anxiety ^b	0.3 (0.4)	0.3 (0.3)	0.5 (0.4)	0.3 (0.4)	0.050	0.383

CES-D, Center for Epidemiologic Studies Depression Scale; POMS, Profile of Mood States; BSI, Brief Symptom Inventory.

^aCPAP (n=24).

^bPlacebo (n=29)