Continuous Positive Airway Pressure Normalizes Cardiac Autonomic and Hemodynamic Responses to a Laboratory Stressor in Apneic Patients*

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Objectives: We examined the effect of continuous positive airway pressure (CPAP) treatment for sleep apnea on cardiac contractility, heart rate variability, and hemodynamics at rest and in response to a laboratory stressor.

Subjects and instrumentation: Forty-one apneic patients were studied on three occasions: before treatment, after 1 full night of CPAP treatment, and after 1 week of CPAP treatment. The subjects were randomly assigned to receive effective treatment or placebo. Contractility and hemodynamics were determined with impedance cardiography, and parasympathetic activity was assessed by analysis of heart rate variability. Measures were determined at rest and in response to a stressor.

Design and results: For the cardiac sympathetic (contractility) measures (preejection period, cardiac acceleration index [CAI], and low-frequency/high-frequency ratio) significant interactions were found in the combination treatment (CPAP vs placebo) by study day (day 1, day 3, day 11) by test period (baseline, preparation, talking) \( p < 0.01 \). For these measures, there were no differences between the treatment groups or responses to the stressor on day 1. Levels in placebo-treated subjects did not change or respond on the subsequent study days. In the CPAP-treated subjects, there was a decrease in these indexes at baseline, which became significantly lower by day 11 (ie, CAI levels were 24 \( \Omega/s^2 \), 22 \( \Omega/s^2 \), and 14 \( \Omega/s^2 \) on day 1, day 3, and day 11, respectively). These measures also became responsive to the stressor by showing increased sympathetic activity (CAI levels on day 11 were 14 \( \Omega/s^2 \) at baseline, 32 \( \Omega/s^2 \) during speech preparation, and 36 \( \Omega/s^2 \) while speaking). The parasympathetic indexes, such as high-frequency power or band of heart rate variability as determined by spectral analysis, showed a significant day-by-treatment interaction \( p < 0.005 \), whereas the CPAP-treated group had significantly more parasympathetic activity after 1 week of treatment. For the hemodynamic measures (stroke volume [SV], cardiac output, and systemic vascular resistance [SVR]), there were significant treatment-by-study day-by-test-period interactions \( p < 0.01 \). SV and cardiac output increased across days, and SVR decreased in the CPAP-treated patients.

Conclusions: These results indicate that CPAP normalizes contractility, increases cardiac vagal tone, and changes hemodynamic regulation from being resistance dominated to being cardiac dominated. Thus, after 1 week of treatment with CPAP, many of the indicators of poor cardiac functioning in apnea patients are improved.

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Key words: autonomic nervous system; continuous positive airway pressure; contractility; heart rate variability; hemodynamics; sleep apnea

Abbreviations: BMI = body mass index; CAI = cardiac acceleration index; CPAP = continuous positive airway pressure; dZ/dt = impedance waveform; HF = high frequency; HR = heart rate; HRV = heart rate variability; LF = low frequency; MAP = mean arterial pressure; NRSA = nonrespiratory sinus arrhythmia; OSA = obstructive sleep apnea; PEP = preejection period; PSG = polysomnography; RDI = respiratory disturbance index; RSA = respiratory sinus arrhythmia; \( \text{SaO}_2 \) = arterial oxygen saturation; SNS = sympathetic nervous system; SV = stroke volume; SVR = systemic vascular resistance

Obstructive sleep apnea (OSA) impairs breathing and leads to repetitive hypoxia and arousal. OSA is associated with hypertension, heart failure, arrhythmia, and death. Patients with sleep apnea frequently show changes in sympathetic nervous system (SNS) activity, such as increased sympathetic nerve firing, an elevation in plasma norepinephrine, diminished \( \beta \)-adrenergic receptor sensitivity, and altered...
cardiac contractility. One study found that apneic patients have elevated cardiac contractility at rest, but they do not respond with further increases in contractility to stress. Parasympathetic changes have also been noted in apneic patients; there is a decrease in vagal activity as noted by diminished high-frequency (HF) heart rate variability (HRV) and decreased baroreceptor sensitivity. Treatment of OSA with continuous positive airway pressure (CPAP) is effective in increasing arterial O₂ saturation (Sao₂) and has been reported to change autonomic tone.

Cardiac β-adrenergic drive alters the relationship between electrical and mechanical systole by accelerating both the rate and force of myocardial contractility. The preejection period (PEP) measures the velocity of isovolumic myocardial contraction, so it is a measure of contractility. PEP correlates highly with left ventricular ejection fraction and the rate of ventricular pressure change. When there is an increase in β-adrenergic drive, the PEP interval decreases. Thus, PEP is inversely related to β-adrenergic drive on the myocardium. Increased β-adrenergic drive shortens the corrected QT interval. A third useful measure of cardiac adrenergic drive is the cardiac acceleration index (CAI), which reflects the acceleration of the rapid ventricular ejection phase after the aortic opening. CAI reflects cardiac contractility during the period maximum velocity of left ventricular ejection. Both CAI and PEP are independent of HR. Because the QT interval is affected by HR, QT adjusted for HR, or QTc, is traditionally used for reporting this measure. The CAI, PEP, and QTc have been useful to estimate myocardial sympathetic drive.

Estimation of the parasympathetic nervous activity in intact systems is difficult. Recognition of the respiratory component of HRV as being vagally mediated resulted in methodologies to assess the respiratory component of HRV as being vagally intact systems is difficult. Recognition of the respiratory component of HRV resulted in methodologies to assess the respiratory sinus arrhythmia (RSA). Spectral analysis is in the range 0.10 Hz; it is associated with the variability because of respiration and parasympathetic activity. The midfrequency power or band is between 0.05 Hz and 0.10 Hz; its activity is undefined. The low-frequency (LF) power or band is between 0.01 Hz and 0.05 Hz; it is not related to respiration, and may represent sympathetic activity. The LF spectrum, however, has also been related to baroreceptor firing. Other investigators described a time-domain technique to assess vagal activity by using an adaptive filtering methodology to quantify the magnitude of RSA and nonrespiratory RSA (NRSAs) influences on HRV. Adaptive filtering decomposes the HR signal based on its correlations with the respiration signal and takes into consideration both the magnitude and the phase of each signal. Therefore, an advantage of adaptive filtering relative to other time-domain methods is that no definition of respiratory spectral bandwidth is necessary because the RSA will contain only the HR that is within the ongoing respiratory frequency.

OSA is associated with hypertension and altered hemodynamics. Apneic patients have higher BP, increased vascular resistance, and decreased cardiac output. In dogs, OSA results in transient increases in nighttime BP and eventually sustained daytime hypertension; arousal alone, at night, did not produce these changes. In general, the BP effects of sleep apnea are greater at night than during the waking hours. Cardiovascular autonomic nervous system changes are markedly impacted by OSA. These changes include increased LF spectral components of BP, HR, and sympathetic nerve activity, and decreased HF spectral components. The increased SNS tone and decreased vagal tone is further evidenced by decreased baroreflex sensitivity, increased catecholamines, and platelet activation.

Treatment of OSA through various methods (eg, CPAP, weight loss, avoiding supine position) reduces nighttime BP, sympathetic nerve activity, LF power, and is associated with increased HF power and baroreceptor sensitivity.

In this study, we assessed the effect of treating sleep apnea with CPAP on the responsiveness of the cardiac contractility, HRV, and hemodynamics at rest and in response to a mild laboratory stressor. Because autonomic nervous system indexes are very sensitive to placebo-treatment effects, we also employed a placebo CPAP-treatment intervention to learn if autonomic changes are mainly attributable to the specific CPAP intervention as opposed to a nonspecific response to treatment.

**Materials and Methods**

*Subjects*

Forty-one subjects were recruited through advertisement and referral from sleep-disorder clinics. Subjects were studied after obtaining written informed consent and were randomly assigned to effective treatment with CPAP or an ineffective level of CPAP treatment (placebo). Twenty-three subjects received CPAP: 13 patients were white, 10 were nonwhite, 17 were men, 6 were women, 8 were mildly hypertensive, and 15 were normotensive. Of the 18 patients in the placebo-treated group, 12 were white, 6 were nonwhite, 16 were men, 2 were women, 5 were hypertensive, and 13 were normotensive. If the patients were receiving antihypertensive medications, they were tapered off the medica-
tion at least 3 weeks before beginning the study. Individuals were classified as hypertensive if their seated screening BP was ≥ 140 mm Hg systolic or 90 mm Hg diastolic based on the average of multiple BP measurements.

**Instrumentation**

Sleep polysomnography (PSG) included central and occipital EEG, bilateral electro-oculogram, submental and tibialis electromyogram, and ECG. Respiration was assessed with nasal/oral airflow, abdominal and thoracic respiratory effort, and oximetry. Sleep was scored according to standard criteria. The respiratory disturbance index (RDI) was quantified as the average number of hypopneas plus apneas per hour of sleep; individuals with an RDI ≥ 15 were classified as apneic.

**CPAP Titration:** Optimal effective nasal CPAP to minimize sleep apnea was defined by conventional manual overnight CPAP titration during monitoring with PSG. After standard PSG hookup, the patient was fitted with an appropriate-sized nasal CPAP mask (Respironics; Monroeville, PA) and slept while the CPAP pressure was maintained at 2 cm H2O. On the appearance of unequivocal obstructive apneas or hypopneas, the CPAP pressure was increased in 2 cm H2O increments until the respiratory events were abolished or until a CPAP pressure of 8 cm H2O was reached.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Placebo Treatment</th>
<th>CPAP Treatment</th>
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<tbody>
<tr>
<td>Age, yr</td>
<td>Mean</td>
<td>SEM</td>
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<tr>
<td>BMI, kg/m²</td>
<td>29</td>
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<td>RDI*</td>
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<td>HR, beats/min</td>
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*CPAP > placebo, p < 0.02.

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![Graphs](image-url)

**Figure 1.** Mean ± SEM of HR (top left, A), QT interval (top right, B), CAI (bottom left, C), and PEP (bottom right, D) responses at baseline and during the preparation and speaking phases of a laboratory stressor. Day 1 is before treatment, day 2 is after 1 full night of treatment, and day 11 is after a full week of treatment. HR was significantly lower in the CPAP-treated group on day 11. QT interval shortened in responses to the stressor. CAI and PEP showed decreased contractility at rest and became responsive to the stressor after 1 week of CPAP therapy. Prep = preparation to speak.
### Table 2—Summary of Significant Statistical Findings of the Univariate Analyses*

<table>
<thead>
<tr>
<th>Variables</th>
<th>BMI †</th>
<th>RDI †</th>
<th>Treatment Condition‡</th>
<th>Day§</th>
<th>Day by BMI</th>
<th>Day by RDI</th>
<th>Day by Treatment</th>
<th>Stress¶</th>
<th>Stress by BMI</th>
<th>Stress by RDI</th>
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<th>Day by Stress</th>
<th>Day by Stress by BMI</th>
<th>Day by Stress by RDI</th>
<th>Day by Stress by Treatment</th>
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<td>3.48 (0.049)</td>
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<td>14.282 (&lt;0.001)</td>
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<td>RSA</td>
<td>6.437 (0.0063)</td>
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<td>SVR</td>
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<td>SV</td>
<td>4.735 (0.0195)</td>
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<td>MAP</td>
<td>35.939 (&lt;0.0001)</td>
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*Data are expressed as F (p value) unless otherwise indicated. For simplicity of reading, only significant terms are reported. df = degrees of freedom.
†As a covariate.
‡Sham CPAP vs active CPAP treatment.
§Study day (day 1 [pretreatment], day 3 [after 1 full night of treatment], and day 11 [after 1 week of treatment]).
¶Stressor period (baseline vs preparation vs talking).
to 10 cm H2O was reached. Further pressure titration was then done in increments of 1 cm H2O based on the presence of apneas, hypopneas, or snoring associated with arousals. Titration was considered ended when most respiratory events were controlled with CPAP while the patient was in the supine position and in the second or third rapid-eye-movement sleep period, or until a pressure of 20 cm H2O had been reached. Placebo CPAP “titration” was administered through a face mask with holes drilled in it, and the pressure was held constant at the initial 2 cm H2O.

Impedance Cardiography: To record the impedance cardiography measures, impedance cardiographic tape was applied in a tetrapolar configuration. The Z2 electrode was attached around the base of the neck, just superior to the suprasternal notch of the thorax. The Z1 electrode was placed 3 cm above Z2. Electrode Z3 used the xiphoid process as an anatomic landmark. The electrode tape was placed over the xiphoid process circumscibing the thorax, keeping the tape parallel to the floor. The Z4 electrode was placed approximately 5 cm below and parallel to Z3. The length between Z2 and Z3 was also determined while the subject stood. After application of the impedance cardiograph electrodes, the ECG electrodes were applied in a modified lead I or lead II configuration that maximized the R wave. The distances between impedance cardiography electrodes 1 and 2, and 3 and 4 were also measured. This spacing was used to place the electrodes on subsequent testing days. ECG electrode placement was similarly measured for consistency of placement each study day.

The ECG and respiration signals (model 78352C; Hewlett-Packard; Andover, MA), Z0 and impedance waveform (dZ/dt) signals (Minnesota Impedance Cardiograph 304B; Surcom; Minneapolis, MN), and BP (Finapres 2300; Ohmeda; Louisville, CO) signals were relayed to an analog-to-digital converter (DT2901; Data Translation; Marlboro, MA), sampling at 1 kHz per channel and stored in a computer. The dZ/dt and Z0 calibration signals were also stored on the computer for later conversion of the dZ/dt to Ω per second and stroke volume (SV) calculations.

These data were collected in 3-min epochs. The samples were ensemble averaged by a computer program that summed the digitized beat-by-beat waveforms, time synchronized to the R wave of the ECG, and divided by the number of cardiac cycles (University of Miami, Behavioral Medicine Research Center). The ensemble average was then graphically displayed and the waveform events were scored by computer signal-processing techniques. SV was calculated using the Kubicek formula.

HRV: We relayed ECG and respiration data and BP data to an analog-to-digital converter (DT2901; Data Translation) sampling at 1 kHz. Data were collected in 3-min epochs using software (Global Lab Software; Data Translation). These samples were stored in a computer for subsequent review, artifact rejection, and calculation. The review and calculation were performed using a program developed at the University of Miami, Behavioral Medicine Research Center.33,34 This program calculated the variables of LF power and HF power from spectral analyses and RSA and NRSA from adaptive filtering. Details of the calculation have been reported previously,33,34

In summary, adaptive filtering is a time-domain measure that permits the temporal tracking of changes in cardiovascular input. The reliability of this measure is very high and compares favorably with another commonly used time-domain method, V-hat.26,27 This index has many advantages: (1) it is free of the susceptibility for violation of stationary assumptions to which the spectral analytic frequency domain methods are subjected; (2) it extracts the variance in HR that is exactly corresponding with the frequency of the ongoing respiratory signal, and thus it is not necessary to a priori define the spectral bandwidth associated with respiration; and (3) it contains the ability to separate correlates from uncorrelated components in signals, where overlapping of the RSA spectra with other lower-frequency components (because of such influences as thermoregulation or BP).

The signals describing the HR fluctuations because of respiration were obtained by decomposing the HR time series using the adaptive filtering technique. The instantaneous HR time series, as well as respiration, were subsampled at a 4 Hz frequency. Because the RSA is correlated with the respiration, while the NRSA is not, the two components can be separated by an adaptive filtering system.34 The respiration signal was processed through a finite impulse response digital filter with adjustable coefficients, such that the filter output was the best estimate of RSA. The difference between the HR time series and RSA was the estimate of NRSA. The NRSA signal was used point by point in an algorithm to adjust the filter coefficients iteratively, such that the filter output had a maximum correlation with the HR time series, while the remaining signal had a minimum correlation with the respiration. In performing the adaptive filtering, the order of the filter was set to p = 10 and the stability and the rate of convergence was controlled by μ = 0.005. The RSA was then calculated as the variance of the estimated respiratory-correlated component. Thus, RSA reflects parasympathetic activity and NRSA reflects sympathetic activity and may include baroreceptor firing, temperature effects, etc.

Scoring of both HRV and impedance cardiogram was performed by a technician who was blinded to the patient and treatment condition.

Procedure

Patients were studied for 11 days. Beginning at 7 AM, day 1 consisted of admission to the Clinical Research Center of the University of California San Diego Medical Center and the first night of sleep PSG, with reactivity testing beginning at 9 AM the following morning. Day 2 consisted of CPAP titration. Day 3 was a full night of sleep with CPAP or placebo treatment and reactivity testing the following morning. On day 4 to day 10, treatment continued at home. On day 11, the patients returned to the Clinical Research Center for sleep monitoring and reactivity testing.

Cardiovascular reactivity testing, as a way to perturb the heart and autonomic nervous system, was performed the mornings of study day 1, day 3, and day 11. Subjects were brought to the laboratory at 9 AM, instrumented, and then allowed to sit quietly for 30 min for habituation to the instrumentation and testing environment. A 3-min baseline was determined at the end of the habituation period. After a 3-min baseline period, the subjects were given instructions for a speaking task. This task involved preparing and presenting a speech in response to one of three situations (accused of shoplifting, automobile dealer not honoring a warranty, and not finding an advertised sale item at a store). These situations were randomly presented to the subject across sessions. Instructions were given that the performance would be videotaped and rated by experts on poise and articulation. The video camera was displayed prominently during the procedure. Subjects were given 3 min to prepare their speech and told that the speech should cover certain points. Immediately after the preparation period, subjects talked for 3 min. If subjects stopped talking before the end of the period, they were reminded to continue the talk by reiterating or summarizing the main points. This speech stressor has been used extensively in our laboratory and other laboratories and elicits reliable changes in the measured parameters (ie, 8, 24, 35, 36, 37).

Data Analysis

The dependent variables were mean arterial pressure (MAP), systemic vascular resistance (SVR), cardiac output, SV, HR, CAI,
PEP, QTc interval, LF power, HF power, NRSA, and RSA. These data were analyzed using a two (treatment CPAP vs placebo CPAP) by three (stress period [baseline, preparation, speaking]) by three (study day [day 1, pretreatment; day 3, one full night of treatment; day 11, after 1 week of treatment]) repeated-measures analysis of variance (SPSS for Windows 9.0; SPSS; Chicago, IL). All p values are reported using the multivariate solution for repeated measures, and Bonferroni corrections were made where appropriate.

### Results

#### Subject Characteristics

Subject characteristics are summarized in Table 1. Subjects in the CPAP condition were significantly larger ($t[40] = -2.671$, $p = 0.011$) and had higher RDI ($t[40] = -2.482$, $p = 0.017$) than the control subjects. Because of these differences, body mass index (BMI) and RDI were used as covariates in the subsequent analyses. As listed in Table 2, these covariates were not statistically significant for any or the quantities studied. The treatment groups did not differ in the average number of hours of CPAP blower time at prescribed pressure used per night (Table 1).

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21961/)

Figure 2. Mean ± SEM LF/HF ratio (top left, A), HF power (top right, B), NRSA (bottom left, C), and RSA (bottom right, D) responses at baseline and during the preparation (prep) and speaking (talk) phases of a laboratory stressor. Day 1 is before treatment, day 2 is after 1 full night of treatment, and day 11 is after a full week of treatment. LF/HF ratio was not different between treatment groups on day 1 or day 3; on day 11, it was lower in the treatment group and increased in response to the stressor. HF power and RSA did not change across days in the placebo-treated group; HF and RSA showed a significant increase from day 1 to day 3 to day 11. NRSA was not affected by treatment, but showed a significant increase in response to the stressor.

Treatment resulted in significant changes in the mean $\text{SaO}_2$ between treatment groups seen by the treatment group-by-study interaction ($F[2,70] = 6.342$, $p = 0.015$). Placebo-treated subjects had average nighttime $\text{SaO}_2$ measurements of 89%, 90%, and 90% across the 3 nights, whereas the CPAP-treated subjects had increased nighttime $\text{SaO}_2$ measurements from night 1 to night 3 and night 11 (89%, 95%, 95%, respectively).

#### Cardiac Autonomic Responses

Cardiodynamic responses are summarized in Figure 1 and Table 2.

**HR:** As shown in Figure 1, top left, A, there was a significant treatment-by-day interaction. HR was lower in the CPAP-treated group than in placebo-treated group on day 11. On all days and in both treatment conditions, HR increased significantly in response to the stressor.

**QT Interval:** As seen in Figure 1, top right, B, the QT interval showed significant shortening in response to the stressor.
CAI: Figure 1, bottom left, C shows a significant treatment-by-day-by-stress interaction. Significant differences were not observed between treatment groups on day 1 (before treatment), nor were there a significant changes in response to the stressors. On day 3, no significant group differences were observed. CAI increased significantly from baseline to preparation for the speaking task in the CPAP-treated group ($p = 0.002$). The CPAP-treated group had a significantly lower baseline than the placebo-treated group ($p = 0.0121$) and responded with a significant increase in CAI ($p = 0.036$). The placebo-treated group showed no significant change.

PEP: Figure 1, bottom right, D depicts a significant treatment-by-day-by-stress interaction. No significant changes in PEP were observed on day 1. On day 3, no significant group differences were observed. PEP decreased significantly from baseline to preparation to speak in the CPAP-treated group ($p = 0.0121$) and responded with a significant increase in CAI ($p = 0.036$). The placebo-treated group showed no significant change.

HRV responses are summarized in Figure 2 and Table 2.

**LF/HF Ratio:** A significant treatment-by-day-by-stress interaction is shown in Figure 2, top left, A. No significant differences were found on day 1 or day 3. On day 11, the CPAP-treated group was significantly lower at baseline than observed during the previous days ($p = 0.0041$) and responded to the stressor with a significant increase ($p = 0.0002$).

**HF Power:** A significant day-by-treatment interaction is shown in Figure 2, top right, B. HF increased significantly in the CPAP-treated group from day 1 to day 3 and day 11 ($p = 0.0035$); no changes occurred in the placebo-treated group. There was significant day-by-stress interaction as well; the CPAP-treated group significantly decreased in HF in response to the stressor on day 11 ($p = 0.002$).

**NRSA:** Figure 2, bottom left, C shows that NRSA increased significantly in response to the stressors.
but was unaffected by treatment or days.

**RSA**: A significant day-by-treatment interaction and day-by-stress interaction were also found as illustrated in Figure 2, bottom right, D. RSA increased significantly in the CPAP-treated group from day 1 to day 3 and day 11 (p = 0.001). The CPAP-treated group had significantly decreased RSA in response to the stressor on day 11 (p = 0.017).

**Hemodynamic Responses**: The hemodynamic responses are summarized in Figure 3 and Table 2.

**SVR**: A significant treatment-by-day-by-stress interaction was found (Figure 3, top left, A). On day 1, there were no significant group differences; SVR increased significantly while speaking (p = 0.038). On day 3 and day 11, SVR was significantly lower in the CPAP-treated group (p = 0.01). SVR increased significantly while speaking in both groups (p = 0.007).

**Cardiac Output**: Figure 3, top right, B shows a significant treatment-by-day-by-stress interaction (p = 0.011). On day 1, there were no group differences or significant changes in response to the stressor. On day 3, no significant differences were observed between treatment groups, but cardiac output increased significantly during preparation in the CPAP-treated group (p = 0.017) and did not change significantly while speaking. On day 11, cardiac output was significantly higher in the CPAP-treated group (p = 0.001) and it increased significantly from baseline to preparation for speaking (p = 0.024) but not while speaking.

**SV**: Figure 3, bottom left, C depicts a significant treatment-by-day interaction. SV was significantly higher in the CPAP-treated group on day 11 (p = 0.004).

**BP**: No significant differences were observed between treatment groups or across study days. BP, as represented by MAP, increased significantly in response to the stressor in both treatment groups, as seen in Figure 3, bottom right, D.

**DISCUSSION**

This study had a number of interesting findings. First, we were able to replicate our previous finding that untreated apneic patients have high cardiac contractility that does not change in response to a laboratory stressor.4 Second, contractility normalizes after treatment with CPAP. Third, cardiac vagal tone is low in apneic patients, but increases with CPAP treatment. Fourth, while BP levels do not change substantially with CPAP treatment, the underlying hemodynamics change. Untreated apneic patients have high SVR and low cardiac output and SV; treatment resulted in increased cardiac output and SV and lowered SVR.

Patients with OSA have greater sympathetic activity at rest.1–7 This was manifested by increased cardiac contractility. We observed an association between sleep apnea and altered cardiac β-adrenergic drive at rest and during a behavioral challenge. In a previously reported study8 we focused on the contractility indexes (PEP and CAI), and reported these measures to be altered in patients with apnea. That study also examined the relationship of hypertension to PEP and CAI. In summary, we found normal subjects (PEP average, 118 ms) and nonapneic hypertensive patients (PEP average, 110 ms) to be significantly higher at rest than apneic patients (90 ms) and apneic hypertensive patients (87 ms). In the population at large, the expected range for PEP is 70 to 180 ms. In response to the speech stressor, we observed that the nonapneic subjects shortened PEP 7 to 10 ms during each segment of the task, whereas the apneic subjects showed no change in PEP. For CAI, the results were similar. All of the study values fell within the observed range of 10 to 70 Ω/s². Both normal subjects and nonapneic hypertensive subjects had average lower resting CAI levels (23 Ω/s² and 25 Ω/s², respectively) than the apneic patients (normotensive subjects, 43 Ω/s²; hypertensive subjects, 45 Ω/s²). Again, the nonapneic subjects both had increases in response to the speech task while the apneic subjects showed a small decrease in CAI (statistically not significant). The alteration of these indexes of β-adrenergic activity at the heart appears to be related to apnea, but not hypertension.

Repeated nocturnal airway obstruction results in hypoxemia and generalized neurohumoral activation.1–7,38–57 We find evidence for increased sympathetic stimulation to the cardiovascular system at rest. A consequence of this adrenergic stimulation is the blunted contractility responses during behavioral challenge.53–57 Treatment with CPAP, however, appeared to reverse this effect. CPAP increased SaO₂ and diminished resting contractility and restored appropriate responses to stressors. Furthermore, during the baseline period, we observed a change from sympathetic dominance to increased vagal influence on the heart. The lowered SVR may have resulted in decreased afterload and, in turn, increased SV and cardiac output.

The poor contractility responses in untreated apnea may be explained by our previous observations of
downregulated β2-adrenergic receptors among apneic subjects.3 The increased sympathetic activity occurring with the apneic episodes was associated with decreased β-receptor number and sensitivity. Therefore, we observed that individuals with sleep apnea were not able to respond to a mild perturbation with increased cardiac β-adrenergic responses, as reflected in PEP and CAI measures of cardiac contractility.

We found that CPAP had multiple effects on cardiac autonomic activity and hemodynamics. There was a normalization of SNS influence manifested in the lowering of contractility indexes, which became responsive to the laboratory challenge. Parasympathetic activity increased as measured by HRV. Finally, treated subjects had increased SV, cardiac output, and decreased SVR. Thus, after 1 week of CPAP treatment, OSA patients with normoxemia had less sympathetic cardiac activity at rest and improved cardiovascular responses to stress.

References


