Cardiogenic Oscillations on the Airflow Signal During Continuous Positive Airway Pressure as a Marker of Central Apnea*

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Therapeutic decisions in patients with sleep apnea (*eg*, adjustment of continuous positive airway pressure [CPAP]) depend on differentiating central from obstructive apnea. Obstructive apnea is defined by cessation of airflow in the presence of continued respiratory effort, which is conventionally inferred from chest wall movement or intrathoracic pressure swings. Cardiogenic oscillations in the airflow have been observed during some central apneas, but there is controversy over whether they correlate with airway patency. The present study investigates whether these oscillations are markers of the absence of respiratory effort (central apnea) without regard to airway patency.

Methods: **We examined 648 apneas in 52 patients undergoing nocturnal polysomnograms and CPAP titrations. Airflow was measured using the output of the CPAP generator, and apneas were identified from reduction of airflow to < 10% for > 10 s. We used only the presence or complete absence of thoracoabdominal motion to classify apneas: obstructive apnea when motion was present (297 apneas); and central apnea if motion was totally absent (351 apneas). Central apneas most often occurred at sleep onset or followed arousal with a big breath. Using only the flow signal, all apneas were examined for the presence of cardiogenic oscillation by an observer blinded to other signals and apnea types.**

Results: **No obstructive apnea showed definite cardiogenic oscillations. In four cases, there was a suggestion of oscillation that was not regular enough to be called cardiac. Sixty percent of central apneas showed clear, regular oscillations at cardiac frequency. Cardiogenic oscillations also were seen intermittently during quiet exhalation in apnea-free periods.**

Conclusion: **The presence of cardiogenic oscillations on the CPAP flow signal is a specific indicator of central apnea and may have a role in self-titrating CPAP algorithms. We speculate that transmission of these cardiac-induced oscillations may relate to the relaxation of thoracic muscles during central apnea and is impeded by high muscle tone during obstructive apnea.**

(CHEST 1999; 116:660–666)

Key words: auto-continuous positive airway pressure; cardiogenic oscillations; central apnea; obstructive sleep apnea syndrome

Abbreviations: BMI = body mass index; CI = confidence interval; CPAP = continuous positive airway pressure; EMG = electromyogram; NPSG = nocturnal polysomnogram; OSAS = obstructive sleep apnea syndrome; REM = rapid eye movement sleep; LOC = left electro-oculogram; ROC = right electro-oculogram; EMG = electromyogram.

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Supported by National Institutes of Health-National Heart, Lung, and Blood Institute grants HL53931 and RR00096, and by grants from Mallinckrodt Nellcor Puritan Bennett and the Foundation for Research in Sleep Disorders.

Dr. Rapoport and Mr. Norman have a financial interest in the development of automatic CPAP in the form of patent rights (assigned to New York University and licensed to Mallinckrodt Nellcor Puritan Bennett).

Manuscript received September 3, 1998; revision accepted March 31, 1999.

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During the therapeutic titration of nasal continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea syndrome (OSAS), residual apneas may occur that can be either obstructive or central. Differentiating these two types of apnea, which have different physiologic as well as therapeutic implications, may impact on the adjustments made to the CPAP pressure. On the one hand, if events are obstructive, it is generally assumed that a higher pressure is needed. In contrast, if the events are central, the optimal response is not clearly defined at the present time, as these apneas may be

transient irregularities of breathing, such as those that occur after arousal[1] or during rapid eye movement (REM) sleep. Not increasing the pressure in the presence of these central events has been recommended as desirable as part of the titration protocol.[2,3] In addition, clinical experience suggests that central apneas may even occur as a reaction to excessive CPAP,[4,5] and this would suggest the need to lower the therapeutic pressure. Alternatively, some central apneas may respond to further increases in CPAP. [6] Irrespective of the decision to raise, lower, or maintain the CPAP when central apnea is detected, the decision can be made (and the impact of the decision tested) only if the apneas are correctly classified.

By definition, both types of apnea are identified by the absence of airflow. Differentiation between them is based on analysis of respiratory effort during the apneic period. This can be done either by noninvasive methods (*eg*, impedance bands) or from direct but invasive measurement of intrathoracic effort (*eg*, esophageal balloon). Of note, both approaches rely on more than the detection of airflow alone.

A frequent incidental finding seen during monitoring of respiratory signals is the presence of cardiogenic oscillations.[7] These have been observed and reported during expiration as well as during apnea. Visible oscillations on the airflow signal during quiet exhalation are frequently seen during measurements made of pulmonary physiology, *eg*, single-breath nitrogen[8] and diffusion studies.[9] The detection of small movements at the cardiac frequency by inductive plethysmography (Fig 1, *bottom*, *C*) or expiratory carbon dioxide signal[10] during apnea has been suggested as an index of their "central" nature. More recently, similar oscillations have been observed on the airflow signal in adults and neonates during central apneas.[11–15] Whereas Lemke et al[12] suggested that the presence of cardiogenic oscillations *always* correlated with a directly visualized open airway, Morrell et al[11] showed that similar oscillations were observed during central apneas regardless of the airway patency. Thus, there is no consensus on whether the presence of cardiogenic oscillations transmitted to the flow signal is dependent on patency of the airway (which can be compromised during the course of a central event) or on lack of respiratory effort.

The present study in patients treated with nasal CPAP was designed to address the question of whether the presence of cardiogenic oscillations on the airflow signal was useful in separating central from obstructive apneas without regard to airway patency.

Materials and Methods

We analyzed 55 unselected nocturnal polysomnograms (NPSGs) (performed sequentially during two time periods) that had been performed with CPAP titration at the New York University Sleep Center. Of these, 3 NPSGs were discarded because no apneas were seen, leaving 52 with at least one apnea, which form the data set for the present analysis. There were 12 women and 40 men. The mean (± SD) age was 48 ± 12 years, and mean body mass index (BMI) was 36 ± 10 kg/m^2. All patients had been diagnosed with sleep-disordered breathing (either OSAS or upper airway resistance syndrome) during a previous diagnostic study (apnea-plus-hypopnea index, 65 ± 40). The prescribed CPAP level was 10 ± 3 cm H_2O.

EEG recordings from central (C3) and occipital (O1) electrodes, left electro-oculograms (LOCs) and right electro-oculograms (ROCs), and submental electromyograms (EMGs) were used to monitor sleep. A unipolar ECG was used for cardiac monitoring. A pulse oximeter (Sensor Medics Corporation; Yorba Linda, CA) monitored oxygen saturation. Nasal mask flow was obtained from a pneumotachograph (Nellcor Puritan Bennett; Minneapolis, MN) within the CPAP circuit, and respiratory effort was monitored by piezoelectric strain gauges (EPMSystems, Inc; Midlothian, VA) on bands detecting chest-abdomen motion. The polysomnographic records were scored for sleep using the criteria of Rechtschaffen and Kales.[16]

In each NPSG, apneic events (absence of airflow for > 10 s) during sleep were identified exclusively from the flow signal from the CPAP generator. In our laboratory, CPAP titration is rapidly accomplished to a level that eliminates apneas, and, thus, only rare obstructive apneas remain for analysis; even during subtherapeutic CPAP, residual obstructive events are primarily hypopneas, which were not relevant to the present study. Despite this, a total of 648 obstructive and central apneas were identified (range, 1 to 102 events in each patient). These were subsequently classified using the following criteria: central apnea was present if no detectable chest or abdominal movement occurred during any part of the event; and obstructive apnea was present if there was any chest or abdominal movement indicating respiratory effort.

These definitions reflect those in general clinical use, especially during CPAP titration, and they are used by most technicians to decide how to adjust CPAP pressure. While the examiner could not be blinded to the presence of cardiogenic oscillations during the apnea, this was not used in defining whether the event was either obstructive or central in nature.

Each apnea was then reviewed for the presence of cardiogenic oscillations on an amplified flow tracing by an observer who was blinded to all other signals and to the earlier apnea classification. Cardiogenic oscillations were defined as visible variations in airflow signal with at least five consecutive oscillations at cardiac frequency. No attempt was made to ascertain airway patency by other techniques.

Events were tabulated, and sensitivity, specificity, positive and negative predictive values, and their confidence intervals (CIs) were calculated for using the presence of cardiogenic oscillations during apnea as an indicator of central apnea. Patients were grouped into those whose central apneas always had cardiogenic oscillations, those whose apneas never had cardiogenic oscillations, and those whose apneas showed variable percentages of cardiogenic oscillations. Differences among the weights, BMIs, ages, and prescribed CPAP levels of patients were tested by Kruskal-Wallis rank analysis of variance. Association between CPAP pressure during each central apnea and the presence of cardiogenic oscillations was tested by Student's *t* test. Association among sleep position (lateral vs supine), sleep stage (REM vs non-REM), and the presence of cardiogenic oscillations were tested by χ^2 test.

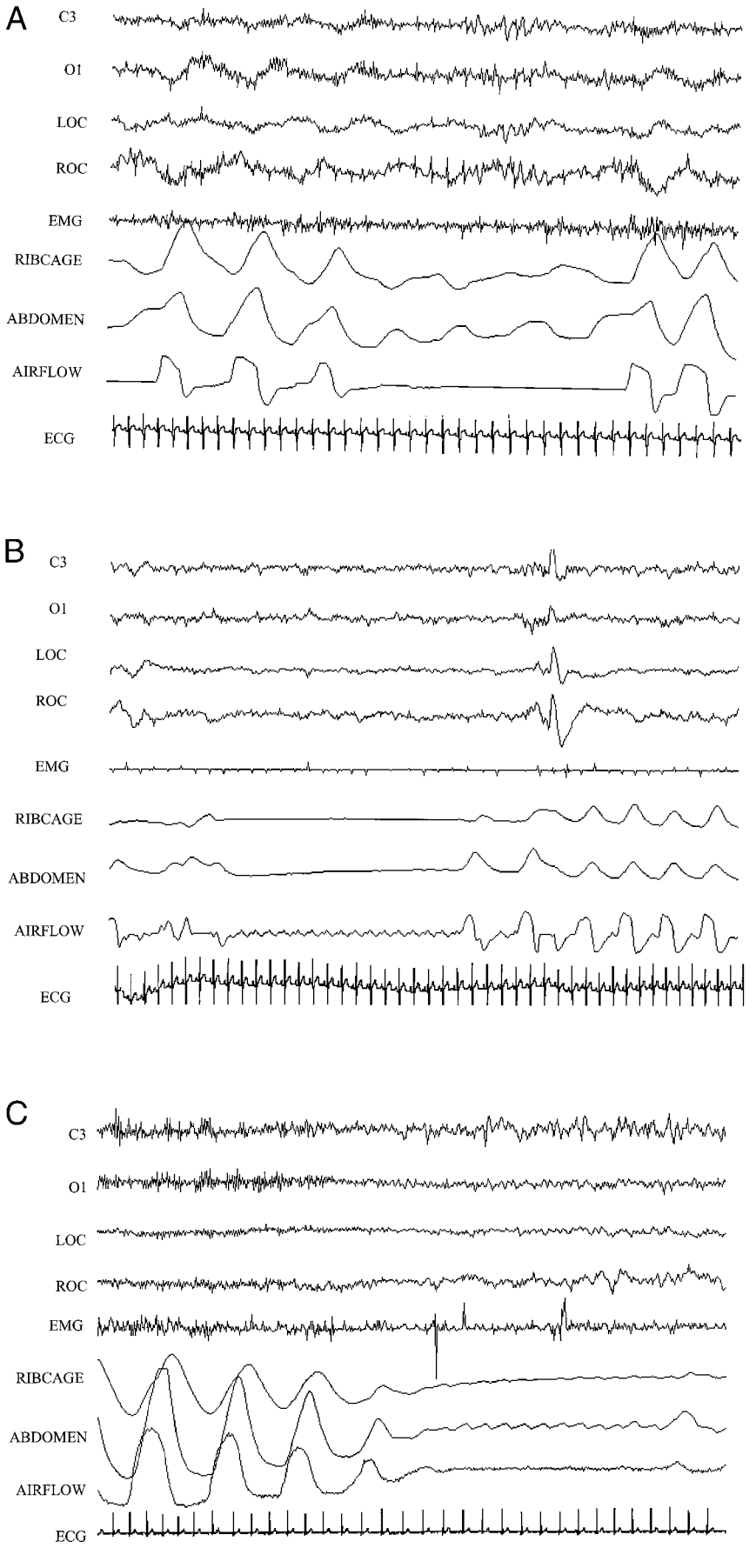

FIGURE 1. Representative events identified on NPSG tracings during CPAP therapy. Channel labels are defined in the "Materials and Methods" section. *Top*: obstructive apnea event (effort on the rib cage and abdomen signals) with no cardiogenic oscillations seen in the airflow signal. *Middle* and *bottom*: central apneic events (no effort on the rib cage and abdomen signals) with and without cardiogenic oscillations, respectively. Cardiogenic oscillations are also visible on the abdomen and rib movement signals (*bottom*).

The protocol was approved by the New York University Institutional Board of Research Associates, and all patients gave informed consent.

Results

All patients had been previously diagnosed with OSAS ([mean ± SD] AHI on prior diagnostic NPSG, 65 ± 40). Before the application of CPAP therapy, all patients had predominantly obstructive apneas and no patient had predominantly central apnea. In the present analysis during the titration of CPAP, 648 apneas were identified and classified by traditional inspection of the effort signals. Of these apneas, 351 were classified as central and 297 as obstructive based on thoracoabdominal movement. No mixed apneas were identified. The majority of the central apneas occurred at sleep onset or after a transient arousal. Figure 1, *top*, *A*, shows a representative tracing of an apnea classified as obstructive. Figure 1, *middle*, *B*, and *bottom*, *C*, show tracings of apneas classified as central *with* and *without* visible cardiogenic oscillations on the flow tracing, respectively.

The mean number of apneas in each subject was 12. In 46 of the 52 subjects there was at least one central apnea. Twenty-nine of these showed both central and obstructive events. Seventeen subjects had only central apneas, and 6 had only obstructive events. Thus, the majority of subjects (56%) had both central and obstructive apneas.

Sixty percent of the 351 central apneas and none of the 297 obstructive apneas showed cardiogenic oscillations (Table 1). In four obstructive apneas there was a suggestion of oscillation, but this did not meet our criterion of five consecutive oscillations at the cardiac frequency. Specificity of using cardiogenic oscillation on the flow tracing to identify central apnea was 100%, and sensitivity was 60%, yielding a positive predictive value of 100% and a negative predictive value of 68%. Figure 2 shows the number and percentage of central apneas with cardiogenic oscillations in each individual patient.

When one restricts the analysis to data from patients who had more than five central apneas (27 patients), 6 patients showed cardiogenic oscillations in all their central apneas, 2 showed cardiogenic oscillations in none of their central apneas, and 19 showed cardiogenic oscillations in 51 ± 19% of their central apneas. In these patients, no pattern emerged with respect to weight, BMI, age, sex, or prescribed CPAP level that differentiated those in whom cardiogenic oscillations were seen consistently (Table 2). There was a nonsignificant trend for patients with lower BMIs to have a higher percentage of central apneas with cardiogenic oscillations.

Table 1—*Classification of Apnea by Presence or Absence of Cardiogenic Oscillations*

	Apnea Type			
	Central*		Obstructive	
Oscillations	No. of Subjects n = 351	%	No. of Subjects n = 297	%
Present	210	60	0	0
Absent	141	40	297	100

*Sensitivity of cardiogenic oscillations, 60% (95% CI, 54.7–65.13); specificity of cardiogenic oscillations, 100% (95% CI, 98.4–100); positive predictive value of cardiogenic oscillation, 100% (95% CI, 97.8–100); and negative predictive value of cardiogenic oscillation, 68% (95% CI, 63.1–72.12).

There was no association between the level of CPAP pressure during the apnea, sleep stage, or body position, and the percentage of central apneas with cardiogenic oscillations (Table 3).

Discussion

The present data show that detection of cardiogenic oscillations on the airflow signal during CPAP titration is a very specific (100%) and a moderately sensitive (60%) indicator of central apnea, as defined by the usual clinical criteria (a cessation of airflow during which no thoracoabdominal movement is seen).The high specificity and high positive predictive value may have important implications for the development and testing of algorithms used in automated titration of CPAP, in which only the airflow signal is readily available. Several algorithms to respond to central apnea can be proposed. CPAP could be raised, lowered, or maintained when central apnea is identified, but a critical step in all algorithms is to differentiate between central and obstructive events if the responses are to be different.

A possible criticism of our methodology is our choice of thoracoabdominal movement as the reference technique used to classify apneas as obstructive vs central. Although the esophageal catheter is the "gold standard" for measurement of effort in diagnostic studies, and its use would have augmented our confidence in the reference classification of apneas, its invasive nature makes it difficult to use in many patients. Thoracoabdominal motion has been used as a practical surrogate for effort in most clinical sleep studies, especially those used to titrate CPAP, and this technique has been reported to be reliable in most situations.[10,17]

Our assessment of the sensitivity and specificity of the use of cardiogenic oscillation to identify central apneas is dependent on the reference classification

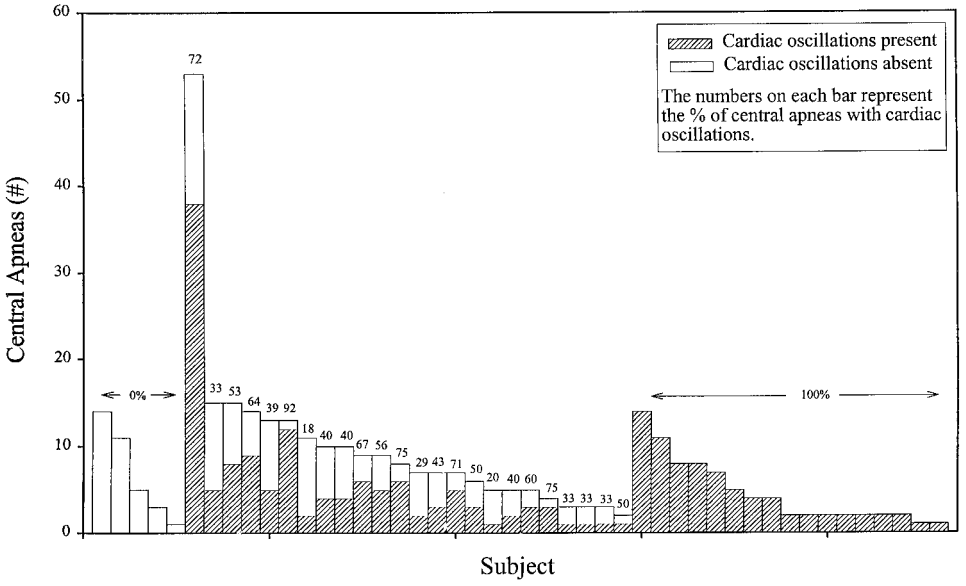

FIGURE 2. Number and distribution of central apneas in each individual patient. Each stacked bar represents one subject and shows the number of central apneas in which cardiogenic oscillations were present and absent. The percentage of central apneas in that subject with cardiogenic oscillations is indicated over each bar.

of each apnea. Misclassification of a truly obstructive apnea as central, due to insensitive detection of thoracoabdominal motion, could have contributed to the low sensitivity (60%) we found but might have raised the specificity artifactually. It seems unlikely to us that truly central apneas would have been misclassified as obstructive by thoracoabdominal movement, as this would have required artifactual movement mimicking respiration. Thus, even with a more definitive classification of events (as with the esophageal catheter), we could only have improved our sensitivity and might have somewhat lowered our specificity. However, despite this limitation, the present study demonstrates diagnostic utility for identifying the presence or absence of cardiogenic oscillations relative to the common clinical standard for classifying apneas during CPAP titration.

The occurrence of *mixed* apneas, *eg*, those that are initially central and become obstructive, poses an additional problem of analysis. Our definition of effort would have forced us to classify these events as obstructive, but no mixed apneas were observed in our data set. This may have been due to the fact that all our patients were on some level of CPAP and that mixed apneas are rare in this setting.[18] Had a mixed apnea occurred, and had cardiogenic oscillations been detected in all or part of its duration, it would have lowered the specificity of our analysis (*eg*, the number of false positives for central apnea would have increased).

There is continuing debate as to the mechanism of transmission of cardiogenic oscillations seen on the airflow signal. Lemke et al,[12] concluded that oscillations were always present in subjects who were awake when the airway was seen to be patent by direct visualization, and were usually present in neonates thought to have central events. Obliteration of oscillations occurred during obstructive events. They concluded that cardiogenic oscillations were an indicator of airway patency but did not verify this

Table 2—*Characteristics of Patients With Central Apnea

Groups (%)†	No. of Patients	Age, yr		BMI, kg/m^2		Sex (No.)	Prescription CPAP, cm H_2O	
		Mean ± SD	Range	Mean ± SD	Range		Mean ± SD	Range
A (0)	2	44 ± 13	35–53	41 ± 6	37–45	M (2)	10 ± 3	8–12
B (51)	19	50 ± 13	17–74	34 ± 5	27–46	M (17) /F (2)	9 ± 3	5–14
C (100)	6	43 ± 13	22–56	29 ± 9	19–43	M (5) /F (1)	8 ± 4	3–14

*Values given as mean ± SD, unless otherwise indicated.
†Patients with central apnea with cardiac oscillations.

Table 3—*Frequencies of Cardiogenic Oscillations During Central Apneic Events With Respect to Body Position, Sleep Stage, and CPAP Level*

Variables	Events With Cardiac Oscillation	Events Without Cardiac Oscillation	p Value
Body position			
Lateral	29.6%	22.2%	0.47
Supine	25.4%	22.9%	
Sleep stage			
REM	7.2%	7.2%	0.40
Non-REM	49.5%	36.1%	
Mean CPAP, cm H_2O	8.4	8.4	0.93

during sleep. The absence of cardiogenic oscillations during all obstructive apneas in our data is in agreement with these findings. Morell et al[11] examined only central apneas and concluded that there was no relationship between cardiogenic oscillations and airway patency. These studies suggest two different ways to explain our 60% sensitivity of finding cardiogenic oscillations in central apnea. First, in accord with the observations of Morrell et al,[11] cardiogenic oscillations may not always occur in the airflow signal, even when the airway is patent. Alternatively, in accord with the observations of Lemke et al,[12] the central apneas seen in our study may have been a mixture of open and closed airway central events; the 60% sensitivity may represent the percentage of events with an open airway. Our data do not allow us to address whether cardiogenic oscillations are present in an unspecified subset of central apneas or are markers of a patent airway but suggest that their presence is an indicator of central apnea (whether or not the airway is patent).

If patency of the airway, as opposed to lack of respiratory effort, were the reason for the presence of cardiac oscillations, one would predict that there would be a relationship between the level of positive pressure in the airway during CPAP (which should splint[19] the airway open at higher pressures) and the occurrence of cardiogenic oscillation during central apnea. However, this correlation was not found in our data (Table 3).

Our data further lead us to speculate that transmission of cardiogenic oscillations to the airflow signal may be affected by relaxation of respiratory musculature, in addition to being influenced by patency of the airway. Thus, high muscle tone during respiratory efforts may alter coupling between the changes in volume due to cardiac contraction and volume changes in the airway. An ancillary finding in our data supports the importance of muscle tone: during quiet breathing, cardiogenic oscillations frequently appear at end expiration (Fig 3) and disappear during inspiration or increase in respiratory effort (*eg*, at arousal). The mechanisms of coupling appear to be complex, and transmission of cardiogenic oscillations to the flow signal at the nose and mouth could even occur *outside* the thorax (*eg*, from major vessels in the neck to the upper airway, above the site of obstruction). This would provide a mechanism by which muscle tone could influence transmission.

In conclusion, the present data show that detect-

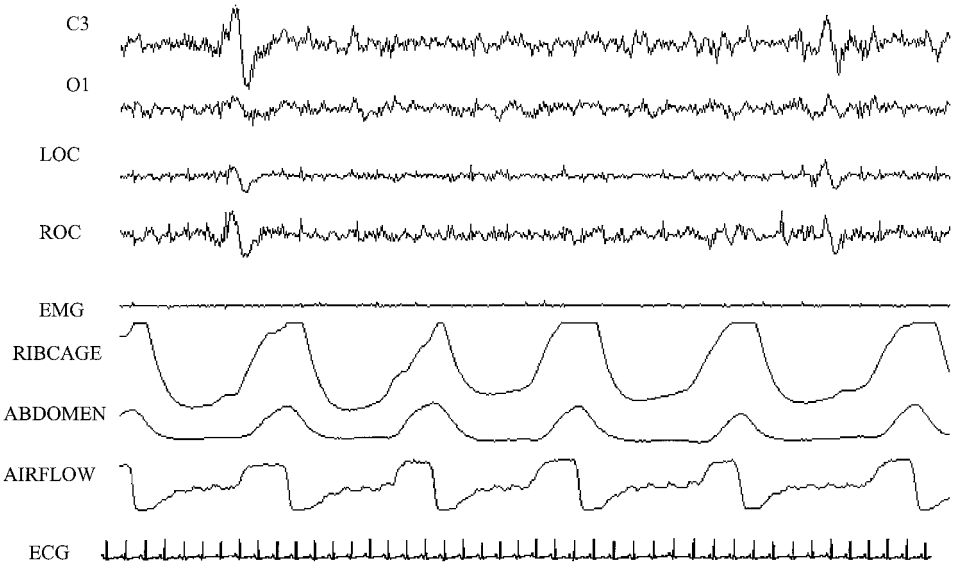

FIGURE 3. NPSG tracing of quiet breathing during sleep on therapeutic CPAP. Cardiogenic oscillations can be seen on the flow signal during exhalation but disappear during inspiration.

ing the presence of cardiogenic oscillations on the CPAP flow signal is a useful indicator of central apnea, as usually defined by the absence of thoracoabdominal motion. We also propose that our technique may have a role in improving algorithms used in automated CPAP titration.

ACKNOWLEDGMENT: The authors wish to acknowledge the assistance of Mohammed M. Ahmed and Rebecca O'Malley in the scoring of the records.

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