Detection of Flow Limitation with a Nasal Cannula/ Pressure Transducer System

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We previously showed that upper airway resistance can be inferred from the inspiratory flow contour during continuous positive airway pressure (CPAP) titration in obstructive sleep apnea syndrome (OSAS). The present study examines whether similar information can be obtained from inspiratory flow measured by a nasal cannula/pressure transducer. Ten symptomatic patients (snoring, upper airway resistance syndrome [UARS], or OSAS) and four asymptomatic subjects underwent nocturnal polysomnography (NPSG) with monitoring of flow (nasal cannula) and respiratory driving pressure (esophageal or supraglottic catheter). For each breath the inspiratory flow signal was classified as normal, flattened, or intermediate by custom software. "Resistance" was calculated from peak inspiratory flow and pressure, and normalized to the resistance during quiet wakefulness. Resistance in all stages of sleep was increased for breaths with flattened (387 ± 188%) or intermediate (292 ± 163%) flow contour. In combination with apnea–hypopnea index (AHI), identification of "respiratory events," consisting of consecutive breaths with a flattened contour, allowed differentiation of symptomatic from asymptomatic subjects. Our data show that development of a plateau on the inspiratory flow signal from a nasal cannula identifies increased upper airway resistance and the presence of flow limitation. In patients with symptoms of excessive daytime somnolence and low AHI this may help diagnose the UARS and separate it from nonrespiratory causes of sleep fragmentation. Hosselet J-J, Norman RG, Ayappa I, Rapoport DM. Detection of flow limitation with a nasal cannula/ pressure transducer system. AM J RESPIR CRIT CARE MED 1998;157:1461–1467.

In the recently described upper airway resistance syndrome (UARS), sleep disruption and symptoms similar to obstructive sleep apnea syndrome (OSAS) result from repetitive increases in airway resistance, which cause frequent arousals from sleep. As originally described by Guilleminault (1) these events were defined by increased intrathoracic pressure swings and occurred with little or no detectable change in the thermistor signal used to monitor airflow.

When a true measurement of airflow is available, as during continuous positive airway pressure (CPAP) titration, we (2) and others (3) have shown that identification of a plateau on the inspiratory waveform correlates with an elevated upper airway resistance. We hypothesized that this would also be true during diagnostic studies without CPAP. However, obtaining a conventional pneumotachograph flow signal requires a tight-fitting face mask, which may be excessively intrusive for routine sleep monitoring. To circumvent this limitation we have been using a simple alternative to the pneumotachograph, which gives a quantitative flow signal without a face mask. This consists of a standard oxygen nasal cannula placed in the nares and attached to a sensitive pressure transducer. This combination detects the pressure fluctuations caused by inspiration and expiration that are proportional to flow. Montserrat has shown that the signal obtained from such a device is comparable in both shape and amplitude to that of a conventional pneumotachograph (4). Additionally we have shown that the nasal cannula detects more events than the thermistor (5) and that these correlate well with the frequent arousals seen in UARS (6). The characteristics of this simple, inexpensive and nonobtrusive device make it ideal for quantitative monitoring of respiration during sleep.

The present study was designed to show that a nasal cannula/pressure transducer system provides a noninvasive indicator of flow limitation (defined by the actual driving pressure/flow characteristics) and that this identifies periods of elevated upper airway resistance in both normal subjects and patients with sleep-disordered breathing.

METHODS

A full night of polysomnography was performed on 10 patients who reported symptoms of sleep-disordered breathing (including excessive daytime somnolence [EDS] and/or severe snoring) and four subjects without these or other sleep complaints. The patient group ($n = 10$) consisted of five patients with obstructive sleep apnea syndrome (EDS and apnea–hypopnea index [AHI] > 20), four patients with UARS (EDS and AHI < 20), and one patient with snoring, no EDS, and an AHI of 6. Six of 10 patients were being treated with nasal CPAP (range, 7 to 13 cm H_2O) but were studied in the present protocol without CPAP. The asymptomatic subjects gave no history of regular snoring or other sleep complaints. Recordings of central and occipital electroencephalogram (EEG), electrooculogram (EOG), and

(*Received in original form August 4, 1997 and in revised form January 6, 1998*)

Supported by grants from NIH-NHLBI (HL53931 and RR00096) and Nellcor Puritan Bennett.

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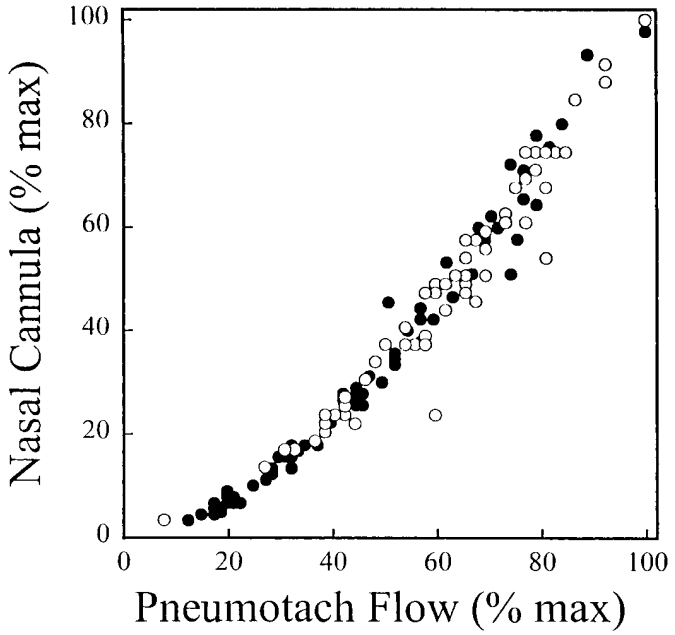

Figure 1. Comparison of signal from the nasal cannula/pressure transducer system used for monitoring respiration and simultaneously obtained pneumotachograph flow from a mask. Awake flow data were collected from two subjects (*open* and *closed symbols*) over a range of breathing patterns and expressed as percent of maximal signal in each subject and in each signal. Flows ranged from 2 to 50 L/min. Overall, the relationship is curvilinear in nature (quadratic as shown by Montserrat and coworkers [4]), but is also nearly linear in the range of normal breathing.

submental electromyogram (EMG) were used to monitor sleep. Sleep was scored using the criteria of Rechtschaffen and Kales (7). Leg movements were monitored with an anterior tibialis EMG. A unipolar electrocardiogram (ECG) was used for cardiac monitoring. Oxygen saturation was monitored with a pulse oximeter. Chest wall and abdominal movement were monitored with piezoelectric strain gauges. Respiratory airflow was simultaneously monitored using a nasal/oral thermistor and a nasal cannula connected to a 2 cm H_2O pressure transducer. In order to justify the use of the nasal cannula signal as "nasal flow," we demonstrated that the relationship between this signal and a simultaneous pneumotachographic flow signal is essentially linear over the relevant range, as was previously shown by Montserrat and coworkers (for our data, *see* Figure 1).

AHI was calculated from the nasal cannula signal using the definition of $>$ 50% (including no flow for apnea) reduction in peak amplitude for $>$ 10 s without regard to the shape of the flow signal (5). Desaturation was not required to confirm an event. The thermistor is used as an ancillary measure. Because of the greater sensitivity of the nasal cannula, which detects 30% more respiratory events in OSAS (5), we have used a cutoff of 20 events/h to separate mild disease from moderate to severe OSAS.

The driving pressure was measured either with a supraglottic or an esophageal catheter. In three subjects a supraglottic polyethylene catheter was placed through one nostril under local anesthetic (lidocaine 2%) and secured in place with tape so that it ended 17 cm from the nares (8). The distal 1 cm of the catheter was perforated with eight lateral holes and the tip was sealed. A bias flow of compressed air ($<$ 0.1 L/min) kept the tube free of secretions. In 11 subjects esophageal pressure was measured with a catheter ending in a 10-cm latex balloon (Ackrad Laboratories, Inc., Cranford, NJ). This was placed transnasally with lidocaine anesthesia, positioned in the lower third of the esophagus, inflated with 1 ml of air and connected to a pressure transducer (Validyne, Northridge, CA). Pressure from either system was taken to represent driving pressure during inspiration.

For each nocturnal polysomnogram (NPSG) the longest possible period of respiration (range, 55 to 451 min) with adequate quality of flow and pressure signals was selected for analysis on a breath-by-breath basis. Each selected period was analyzed using custom-written computer software that identified breaths (n = 47,685) and classified them exclusively by the shape of the flow-time waveform without regard to the amplitude criteria used to define hypopnea (*see above*). If inspiration was found to be sinusoidal in shape, the breath was classified as "normal." If the breath was found to have a flattened contour, it was classified as "flattened." If neither criteria was met the breath was classified as "intermediate."

In addition, for each breath "resistance" was calculated from the peak inspiratory flow and peak pressure during that inspiration (with-

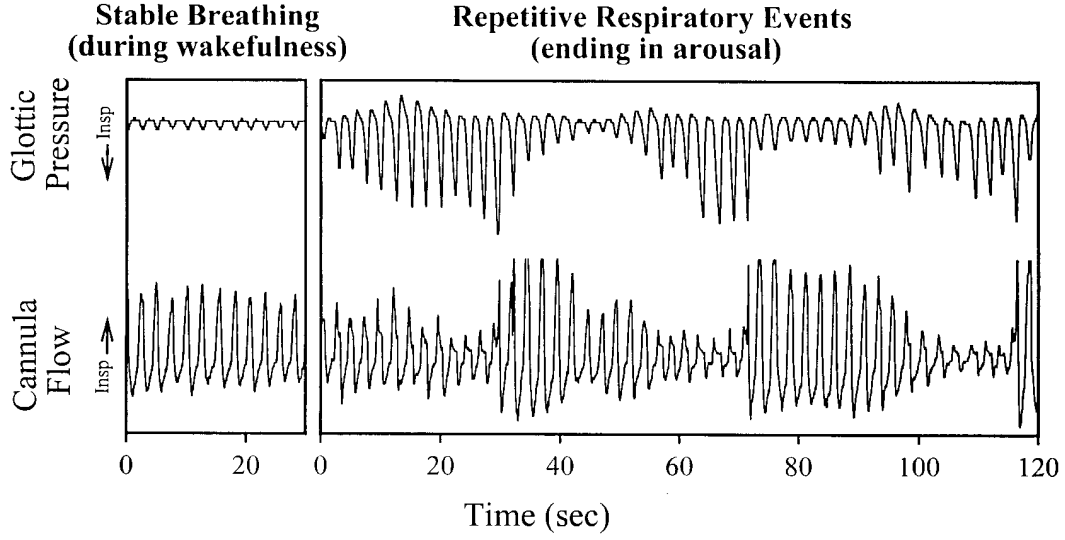

Figure 2. Continuous tracing of flow and supraglottic pressure in one patient with OSAS. *x*-Axis shows time in seconds. *y*-Axes are airflow (inspiration up) and driving pressure (inspiration down). During stable breathing during wakefulness, driving pressure swings are low and the inspiratory flow contour is rounded (*left panel*). During sleep there are repetitive events ending in arousal (*right panel*). The increased swings of the glottic pressure coincide with development of a flattened inspiratory flow/time contour. This occurs even before a significant decrease of the inspiratory flow.

TABLE 1

DEMOGRAPHIC, SYMPTOM, AND RESPIRATORY DATA

	Age (*yr*)	BMI (kg/m^2)	Snoring /EDS	ASDA Arousals (*per h*)	AHI (*per h*)	Breaths Analyzed	Breath Shape		
							% Normal	% Int	% Flattened
Symptomatic subjects									
1	69	26	+/+	24	17	2,229	66	3	31
2	39	35	+/+	24	19	3,293	47	3	50
3	32	33	+/+	37	20	1,620	66	4	30
4	40	42	+/+	33	72	1,466	82	10	8
5	55	26	+/+	27	28	2,825	58	14	28
6	57	27	+/+	22	22	1,745	46	21	33
7	62	28	+/+	24	16	1,342	53	13	34
8	41	25	+/+	23	36	5,200	57	16	27
9	45	36	+/+	52	57	4,324	57	24	19
10	29	23	+/−	23	6	6,987	62	11	27
Mean	47	30		29	29	3,406	59	12	29
Range	29–69	23–42		22–52	6–72	1,342–6,987	46–82	3–24	13–50
Asymptomatic group									
11	47	23	−/−	17	5	5,318	60	13	27
12	27	23	−/−	21	5	3,153	77	10	13
13	24	18	−/−	17	2	7,072	79	4	17
14	25	24	−/−	14	2	1,111	77	10	13
Mean	31	22		17	4	4,163	73	9	17
Range	24–47	18–24		14–21	2–5	1,111–7,072	60–79	4–13	13–27

out regard to relative phase). Because there is no unique resistance during flow-limited breaths, we arbitrarily chose this method as a quantification of the magnitude of airway collapsibility. Furthermore, since our flow signal was not calibrated, for each subject we referred each measurement of resistance to the resistance for that subject obtained during a period of quiet respiration during wakefulness (which was defined as a resistance of 100% for that subject).

For each subject, mean and standard error of resistance were tabulated by breath shape for all breaths in the entire night and separately for breaths during each sleep stage. Cumulative results were tabulated for all subjects for the entire night and for each sleep stage by breath shape. Comparison between resistances was performed by repeated measures analysis of variance (ANOVA) with Tukey's honest significant difference (HSD) *post hoc* analysis.

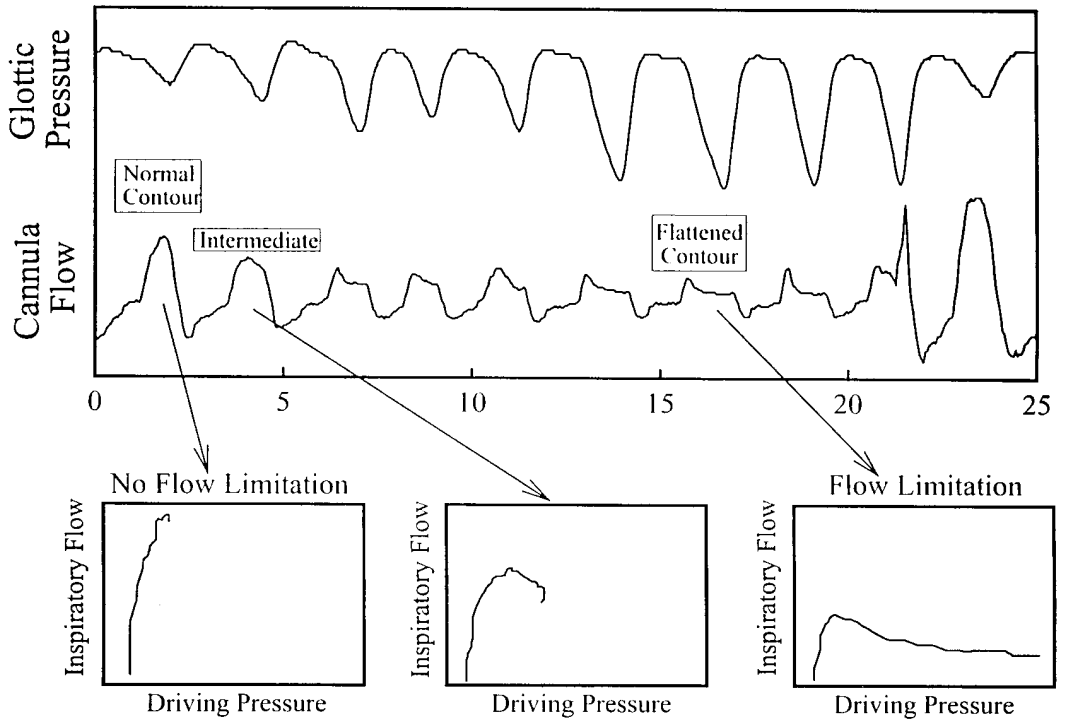

Figure 3. Pressure/flow relationships during a single respiratory event. The *x*-axis shows time in seconds. Breaths with normal, intermediate, and flattened flow contours are labeled and a plot of the driving pressure/flow relationship is shown. The flattened flow/time contour breath shows a nonlinear flow/pressure relationship characteristic of flow limitation.

Finally, the nasal cannula signal was analyzed to identify "events" characterized by a sequence of at least two successive breaths all of which showed flattening of the inspiratory flow contour (which generally lasted more than 10 s). A flattened contour breath event index was calculated as the number of these events per hour of sleep for each subject. The protocol was approved by the New York University Institutional Board of Research Associates and all patients gave informed consent.

RESULTS

Demographic and sleep-disordered breathing characteristics for the symptomatic patients and asymptomatic subjects are shown in the table. The mean AHI was 29/h (range, 6 to 72) for the patients and 4/h (range, 2 to 5) for the asymptomatic subjects. All patients complained of snoring and all but one of excessive daytime somnolence (*see* Table 1). All asymptomatic subjects denied any snoring or EDS.

Figure 2 illustrates data from one patient showing the driving pressure (supraglottic pressure) and flow during two periods. In quiet breathing during wakefulness the supraglottic pressure swings were low and the inspiratory flow contour was rounded (*left panel* of Figure 2). After the onset of sleep, repetitive respiratory events developed during which supraglottic pressure swings became greater while flow decreased; during these events the inspiratory flow/time contour became flattened (*right panel* of Figure 2). Figure 3 shows one of these respiratory events with three different flow/time contours labeled (normal, intermediate, and flattened). Below each labeled flow/time curve the plot of driving pressure/flow is shown for that breath. The normal (rounded) flow/time contour breath has a linear flow/pressure relationship, indicating that it acts like a rigid tube with fixed resistance. For the flattened flow/time contour breath, the flow/pressure plot shows the nonlinear relationship that is characteristic of flow limitation, indicating that it acts like a collapsible tube or Starling resistor. The intermediate breath shows a nonlinear flow-limited pattern that is less pronounced than that for the flattened breath.

The table shows the number of breaths computer-classified by shape for each subject. In total, 10,068 breaths were classified as flattened, 30,264 as rounded, and 5,352 as intermediate. The symptomatic group of patients showed a significantly greater percentage of flattened breaths than did the asymptomatic group (29 ± 10% versus 17 ± 7%, $p < 0.05$). Figure 4 shows summary data for each subject of the resistances of breaths classified by shape. As can be seen, the classification of shape as intermediate or flattened predicted an elevated resistance. The resistance of normal breaths during sleep was 241% (164 to 318%, 95% confidence interval [CI]) of the resistance of breaths during quiet wakefulness. The resistance of the intermediate breaths was 292% (197 to 387%, 95% CI), and the resistance of the flattened breaths was 387% (278 to 496%, 95% CI) of the resistance of breaths during quiet wakefulness. All these differences were statistically significant (ANOVA $p <$ 0.05 with all pairs significantly different by Tukey's HSD *post hoc* analysis).

Only 1 of 14 subjects showed breaths with a flattened contour that did not have a higher resistance than his normal breaths. In this subject (number 13) inspection of the driving pressure curve revealed a nonsinusoidal pattern of respiratory drive that was mirrored in the flow signal. This resulted in a linear driving pressure/flow relationship, without an elevation of resistance, despite the flattened flow/time contour. In this subject, this finding was present throughout all of the recorded breathing, both awake and asleep.

Figure 5 shows the resistance of breaths with the various contours as a function of sleep stage pooling data from all subjects. As can be seen, in each sleep stage the resistance of the abnormal contour breaths was significantly ($p < 0.05$) higher than the resistance of the breaths with normal contour. It can also be seen that, as expected, the resistance during all stages of sleep of even the normal breaths was higher than the resistance seen during awake quiet breathing (i.e., all resistances during sleep were greater than 100%). The highest resistances were seen during Stage 2 sleep. This was true for breaths with both normal and abnormal contours.

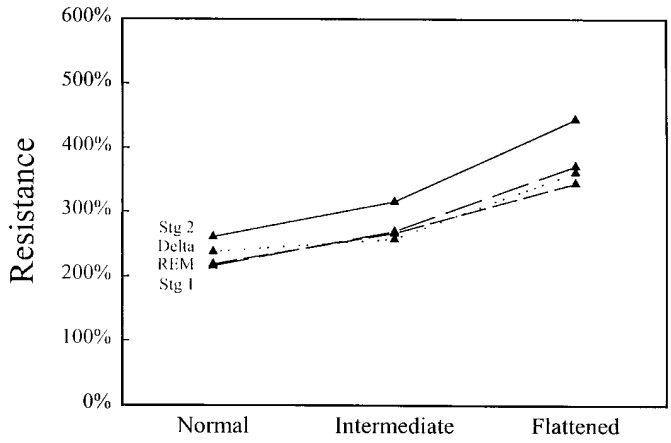

Figure 4. Summary data on resistance for 14 subjects as a function of breath contour. Each point represents the mean value of resistance relative to that of the subject's resistance during quiet respiration during wakefulness (not shown on figure). In all but one subject the resistance of intermediate and flattened contour breaths was higher than that of normal rounded contour breaths.

Figure 6 replots the data of Figure 5 separating symptomatic and asymptomatic subjects. For all breath contours and for all sleep stages, symptomatic subjects had higher resistance. In addition the magnitude of the increase between normal and abnormal contour breaths was greater in the symptomatic than in the asymptomatic subjects although the proportional increase was similar in both groups.

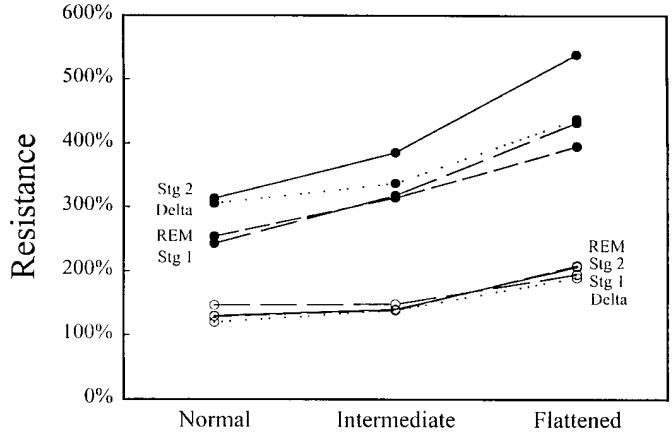

Figure 5. Summary data on resistance as a function of sleep stages and breath contour. The resistance during all stages of sleep of all breath contours was higher than the resistance seen during awake quiet breathing (> 100%). In each sleep stage the resistance of the abnormal contour breaths was higher than the resistance of the breaths with normal contour.

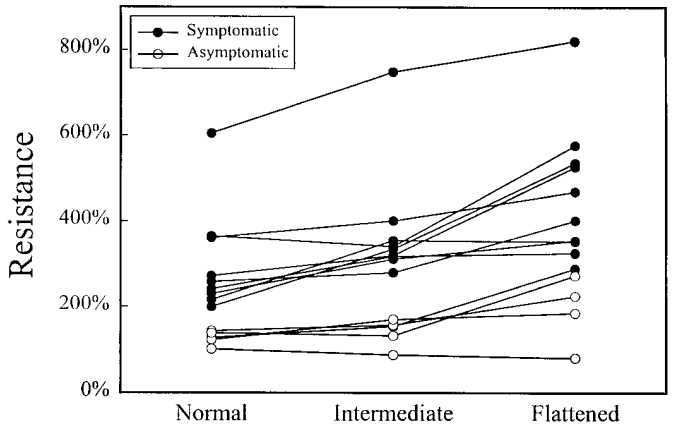

Figure 6. Summary data on resistance as a function of sleep stages and breath contour separating asymptomatic (*open circles*) from symptomatic subjects (*closed circles*). For all breath contours and for all stages, symptomatic subjects exhibited higher resistance.

The difference between symptomatic and asymptomatic subjects is further shown in Figure 7. This figure plots the number of flattened contour breath events per hour of sleep against the AHI. As can be seen, symptomatic subjects with low AHI (< 30/h) had an elevated flattened contour event index (> 30/h). Asymptomatic subjects had up to 26 flattened contour breath events per hour but had low AHIs. Thus one can define on the figure a region bounded by an AHI < 15/h and flattened contour breath events < 30/h (*see dashed rectangle*). This region clearly identified asymptomatic subjects and separated them from symptomatic subjects in our data.

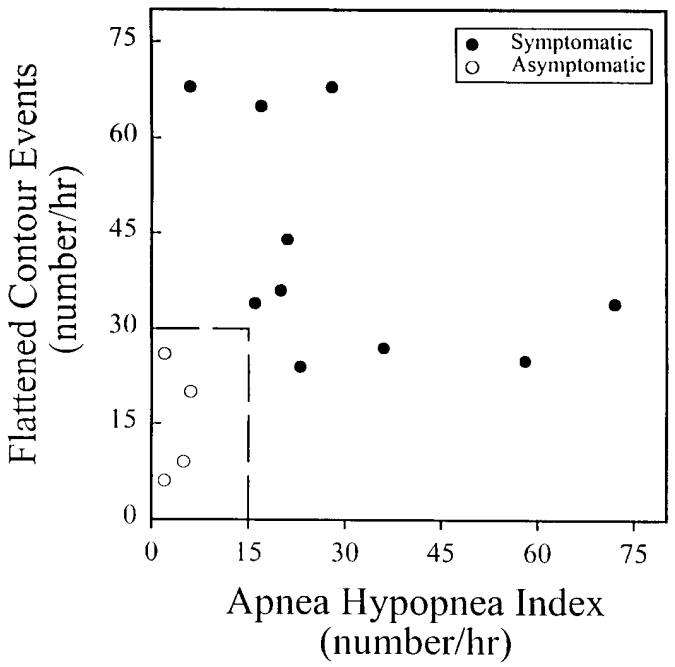

Figure 7. Plot of flattened contour breath events per hour of sleep against AHI in asymptomatic (*open circles*) and symptomatic subjects (*closed circles*). The region defined by AHI < 15/h and flattened contour breath events < 30/h includes all asymptomatic subjects and excludes all symptomatic subjects.

Whereas the increase in resistance from normal to abnormal contour breaths was similar in rapid eye movement (REM) and non-REM, the peak driving pressure seen during REM was often low in association with a low flow. An example of the pressure/flow relationship seen in two breaths during a REM-related event is shown in Figure 8. Although the breath on the right is flow-limited, the peak pressure achieved (-4 cm H_2O) is smaller than during a normal breath (-7 cm H_2O). Thus for some breaths in REM, driving pressure alone did not identify high resistance (calculated from the low driving pressure and flow). This high resistance could be inferred noninvasively from flattening of the inspiratory flow/time contour alone.

DISCUSSION

In this study, we have shown that the inspiratory flow/time contour measured with a nasal cannula/pressure transducer system varies with the level of upper airway resistance and with the presence of flow limitation as defined by the flow/pressure tracing. This occurred whether or not hypopnea was present. Thus a characteristic flattened flow/time contour is indicative of the highest resistance and the presence of flow limitation. In contrast, a rounded flow/time contour is indicative of lower resistance and absence of flow limitation. These observations were true in both symptomatic and asymptomatic subjects and in all sleep stages, with the greatest rises in resistance occurring in patients in Stage 2 sleep.

Respiratory signals are conventionally monitored during polysomnography (NPSG) with a thermistor, which measures temperature as a surrogate of flow. This approach does not allow analysis of the flow/time contour. In the present study we used a simple pneumotachograph (nasal cannula/pressure transducer system) to noninvasively measure flow. This provided a signal whose flow/time contour could be analyzed to detect breaths with elevated resistance (*see* Figure 1). Montserrat and coworkers (4) showed that correlation between this signal and a pneumotachographic flow signal can be improved by a square root transform, but classification of breath types by our computer algorithm is not significantly affected by this difference. Moreover, leaving the flow signal untransformed tends to exaggerate the difference between small and large breaths, which increases the sensitivity of detection of hypopnea by amplitude criteria alone. This may partially account for the increased sensitivity of the nasal cannula technique compared with a thermistor, even without incorporating flow limitation analysis. In our laboratory, because of the greater sensitivity of the nasal cannula, which detects 30% more respiratory events in OSAS (5), we have used a cutoff of 20 events/h to define the syndrome of obstructive sleep apnea/hypopnea. In fact, this definition may tend to blur the distinction between UARS and mild or positional apnea but does not alter the separation of mild disease from moderate to severe OSAS.

In our data the flow/time contour was generally rounded and did not exhibit flattening during quiet breathing while awake. At sleep onset resistance increased in both symptomatic and asymptomatic subjects as has been reported by others (9–12). This occurred in breaths of all shapes and the rise in resistance was significantly greater in the symptomatic group. Both symptomatic and asymptomatic subjects showed some breaths with flattened flow/time contours during sleep and these were associated with further increases in resistance. This may reflect the changes in collapsibility of the upper airway during sleep. In general, the asymptomatic subjects showed both less flow limitation and less increase in resistance during abnormal shaped breaths than the symptomatic subjects. How-

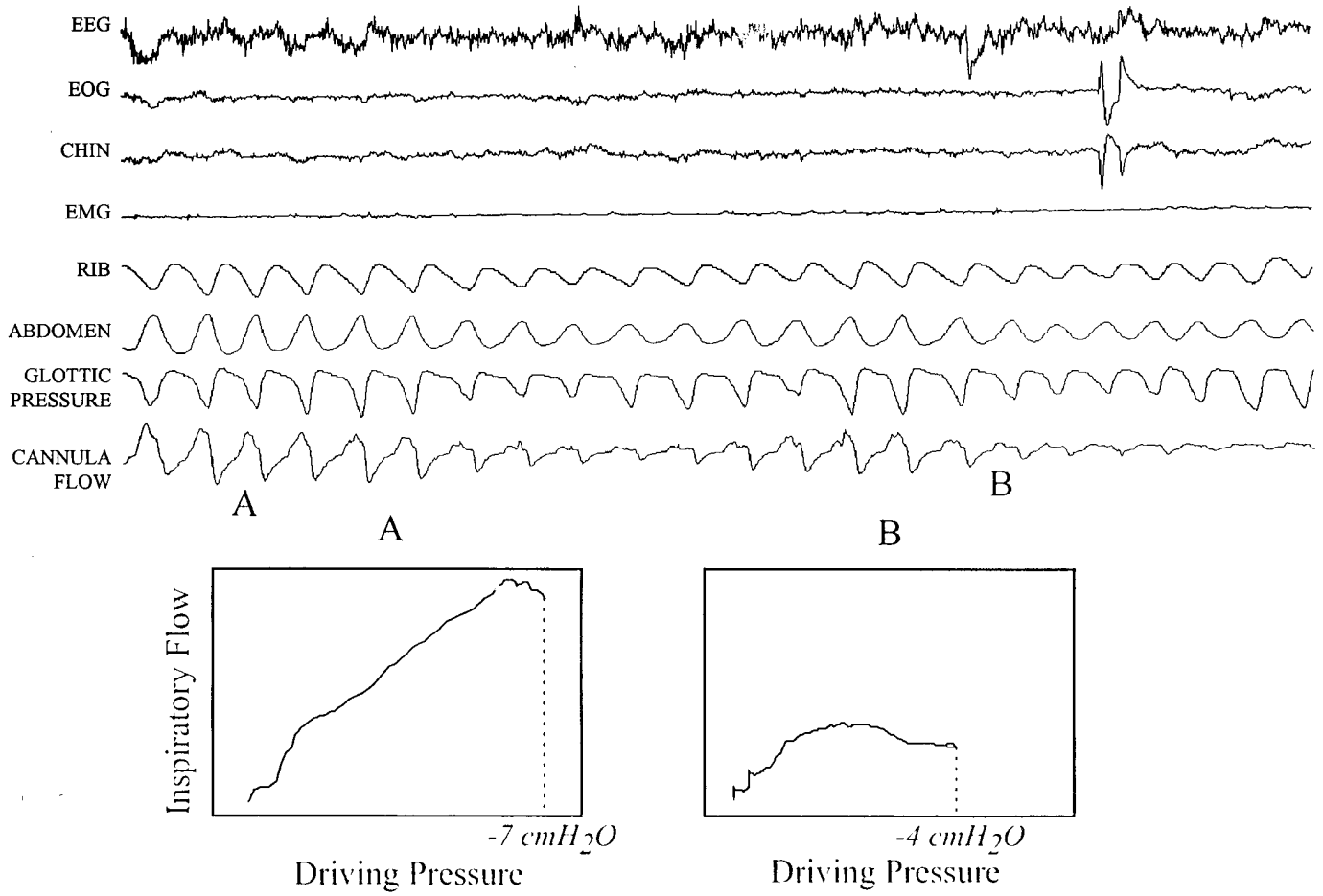

Figure 8. Respiratory events during REM sleep. *Upper panel* shows 60 s of NPSG including flow/time curve (*lowest tracing*). *Lower panel* shows flow/pressure plot for two selected breaths marked A and B. Normal contour breath (*A*) showed a linear flow/pressure relationship. Despite lower driving pressure, the appearance of flattened flow contour (*B*) was associated with flow limitation on the flow/pressure tracing.

ever, when present even in these asymptomatic subjects, the flattened flow/time curve identified the periods of highest resistance in both non-REM and REM sleep. The one exception was Subject 13 who showed a flattened flow/time contour associated with a nonsinusoidal (flattened) driving pressure/time contour, and this may represent an infrequent limitation to our approach. To date this is the only individual we have seen with this phenomenon.

Guilleminault has suggested that respiratory events characterized by elevated swings in esophageal pressure and their consequences may explain the symptoms of UARS. Our data suggest that sequences of breaths with a flattened flow/time contour detect these same events. We have previously shown that sequence of breaths with flattened inspiratory flow/time contour (suggesting events of flow limitation) usually terminate in arousal (6) and have autonomic consequences similar to apneas (9). In addition, detection of flow limitation may provide supplementary information. In REM sleep, where effort-related pressure swings are often low, either the flattened flow/time contour or calculation of resistance may identify significant additional events missed by the analysis of esophageal or driving pressure alone.

There was an overlap in the flattened contour breath event index between asymptomatic subjects and patients with severe OSAS. In severe OSAS the majority of obstructive events are characterized by near zero flow, thus precluding the presence of flow limitation. Despite this, when *both* flattened contour breath event index and AHI were considered, all symptomatic subjects, whether OSAS or UARS, could be separated from asymptomatic subjects.

A technical consideration can be raised about the significance of the pressures measured by an esophageal catheter. While the glottic catheter measures only the pressure related to airway resistance, with an esophageal catheter one needs to consider resistive and elastic components. In the present study we used the *change* of esophageal pressure from inspiration to expiration to calculate resistance. Thus elastic tissue forces drop out except for those due to inspired volume. Because normal breaths tend to be larger than flow-limited breaths (which are also partially obstructed), any elastic contribution to pressure will attenuate the differences in resistance we find between breath types. Thus our results underestimate the degree of variation in resistance between abnormal contour and normal breaths.

In conclusion, the shape of the signal recorded from a nasal cannula can be used as a noninvasive indicator of elevated upper airway resistance and the presence of flow limitation defined by driving pressure/flow characteristics. In patients with symptoms of excessive daytime somnolence and low AHI, where standard thermistors do not reliably detect the characteristic airway events, this approach may help diagnose the upper airway resistance syndrome and separate it from nonrespi-

ratory causes of sleep fragmentation. Thus, we propose that flow limitation events, defined by the presence of successive breaths with a flattened flow/time contour, have a role in defining the spectrum of sleep-disordered breathing.

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