Patient-ventilator interaction and sleep in mechanically ventilated patients: Pressure support versus proportional assist ventilation*

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Objectives: **To understand the role of patient-ventilator asynchrony in the etiology of sleep disruption and determine whether optimizing patient-ventilator interactions by using proportional assist ventilation improves sleep.**

Design: **Randomized crossover clinical trial.**

Setting: **A tertiary university medical-surgical intensive care unit.**

Patients: **Thirteen patients during weaning from mechanical ventilation.**

Interventions: **Patients were randomized to receive pressure support ventilation or proportional assist ventilation on the first night and then crossed over to the alternative mode for the second night. Polysomnography and measurement of light, noise, esophageal pressure, airway pressure, and flow were performed from 10 pm to 8 am. Ventilator settings (pressure level during pressure support ventilation and resistive and elastic proportionality factors during proportional assist ventilation) were set to obtain a 50% reduction of the inspiratory work (pressure time product per minute) performed during a spontaneous breathing trial.**

Measurements and Main Results: **Arousals per hour of sleep time during pressure support ventilation were 16 (range 2–74) and 9 (range 1–41) during proportional assist ventilation ($p = .02$). Overall sleep quality was significantly improved on proportional assist ventilation ($p < .05$) due to the combined effect of fewer arousals per hour, fewer awakenings per hour (3.5 [0–24] vs. 5.5 [1–24]), and greater rapid eye movement (9% [0–31] vs. 4% [0–23]), and slow wave (3% [0–16] vs. 1% [0–10]) sleep. Tidal volume and minute ventilation were lower on proportional assist ventilation, allowing for a greater increase in $Paco_2$ during the night. Patient-ventilator asynchronies per hour were lower with proportional assist ventilation than with pressure support ventilation (24 ± 15 vs. 53 ± 59; $p = .02$) and correlated with the number of arousals per hour ($R^2 = .65$, $p = .0001$).**

Conclusions: **Patient ventilator discordance causes sleep disruption. Proportional assist ventilation seems more efficacious than pressure support ventilation in matching ventilatory requirements with ventilator assistance, therefore resulting in fewer patient-ventilator asynchronies and better quality of sleep. (Crit Care Med 2007; 35:1048–1054)**

KEY WORDS: sleep; weaning; pressure support ventilation; proportional assist ventilation; patient-ventilator interaction

Patients on mechanical ventilation describe sleep deprivation as a major source of physical and psychological stress (1). Moreover, sleep disorders in mechanically ventilated patients may lead to apathy, confusion, and delirium (2), potentially contributing to the development of severe anxiety and depression (3). Although the significance of sleep disruption in this setting is well recognized (4), strategies aimed at improving sleep in mechanically ventilated patients have met with limited success since the etiology of sleep disturbance in the critically ill is still not fully understood (5–7).

Recent data suggest that mechanical ventilation may influence sleep in the critically ill (4). Meza et al. (8) and Parthasarathy and Tobin (9) showed that pressure support ventilation (PSV) caused arousals and awakenings due to central apneas in healthy subjects and in mechanically ventilated patients, respectively. Fanfulla and coworkers (10) showed that when PSV was set taking into consideration inspiratory muscle effort, the rate of patient-ventilator asynchronies decreased and the quality of sleep improved. Patient-ventilator asynchrony has therefore been hypothesized as one of the potential mechanisms responsible for sleep disruption (11).

Proportional assist ventilation (PAV) is a mode of partial ventilatory support in which the ventilator applies pressure in proportion to the inspiratory effort (12, 13). During PAV, patient-ventilator synchrony may be optimized since both the amplitude and time course of ventilator assistance are linked to the amplitude and time course of inspiratory effort. A recent clinical trial demonstrated that PAV is associated with more rapid improvement in physiologic variables and is

*See also p. 1202.

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better tolerated than PSV (14); in normal volunteers, PAV is associated with less periodic breathing and sleep fragmentation than PSV (8).

The aim of the study was to assess quality and quantity of sleep during PSV and PAV. We hypothesized that patient-ventilator asynchrony is related to sleep disruption.

METHODS

Patients were recruited from the intensive care unit (ICU) of the San Giovanni Battista-Molinette Hospital (University of Turin). The ethics committee approved the protocol, and written informed consent was obtained from all subjects.

All patients between 18 and 75 yrs of age mechanically ventilated for ≥3 days and sedated with midazolam, lorazepam, or propofol according to the daily interruption protocol at doses not higher than 0.05, 0.01, and 2 mg/kg/hr, respectively, were eligible to participate in the study (15, 16). Once identified, patients were prospectively followed until they met the following inclusion criteria: a) the patient had an intact respiratory drive with a maximal inspiratory pressure >-20 cm H_2O; b) the patient had a Pao_2/Fio_2 ratio >200 on positive end-expiratory pressure (PEEP) ≤5 cm H_2O; c) the patient had a pH of 7.35–7.45; d) sedation had been discontinued for a minimum of 36 hrs for propofol and 72 hrs for lorazepam; e) analgesia was provided solely with morphine at a dosage ≤0.01 mg/kg/hr (16); f) the patient was fully alert and cooperative with a Glasgow Coma Scale score ≥10 (17). Patients were excluded if they a) successfully completed a spontaneous breathing trial (16); b) had an abnormal electroencephalogram performed 24 hrs before study entry; c) had a history suggestive of central sleep apnea or drug or alcohol abuse or had general anesthesia within 72 hrs from study entry, requiring haloperidol >10 mg/24 hr; d) were hemodynamically unstable or had infection, sepsis, severe sepsis, or septic shock (16). Patients could be withdrawn from the study at any time for the following *a priori* defined conditions: a) need for inotropic support, sedation, or analgesia with morphine at a dosage >0.01 mg/kg/hr; b) readiness for extubation (17); c) hemodynamic instability, arrhythmia, Pao_2/Fio_2 ratio <200, pH <7.35 or >7.45, or temperature >37.5°C (18).

Patients were studied in a 12-bed ICU, arranged as a row of three rooms with four patients per room. Each room has the same organizational layout, with one door accessing the common hallway and one wall containing large windows facing east; two beds are positioned adjacent to the window and two beds adjacent to the hallway. Each bed receives the same ambient light. Patient-care activities occur according to set schedules, and lights are generally turned off at 11 pm. Recordings of light and noise during the study were used as surrogate measures for healthcare provider/patient interactions. No changes were made to the drug regimens of patients during the study.

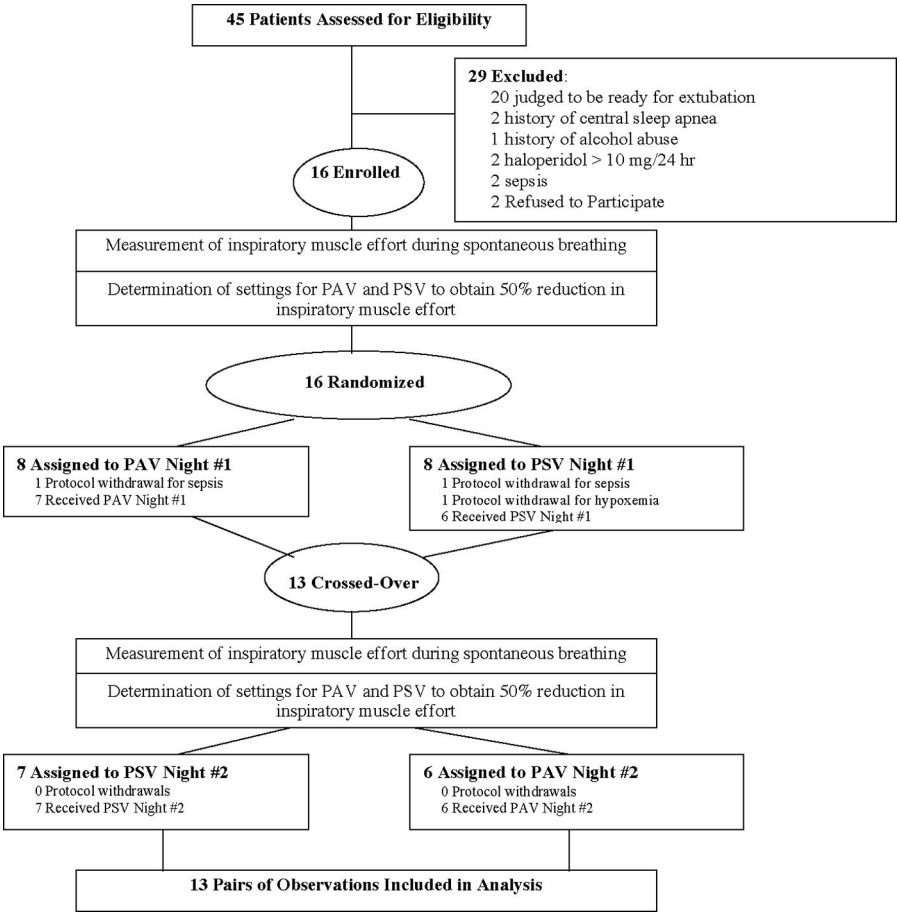

Figure 1. Patient flow diagram. *PAV*, proportional assist ventilation; *PSV*, pressure support ventilation.

Patients were randomized to receive either PSV or PAV (Evita 4, Dräger, Lübeck, Germany) on the first day and then crossed over to the alternate ventilatory modality on the second day; randomization and ventilator setup were performed at 9:00 am (Fig. 1). Ventilator settings were checked at 9:00 pm. Except for Fio_2 and PEEP, no adjustments in ventilator settings were allowed during the night. The following day, the procedure for assessment of ventilator settings for the alternate mode of ventilation was repeated. Inspiratory triggering threshold was set at the most sensitive level not associated with auto-triggering; inspiratory triggering and alarm thresholds were the same for both nights. PSV pressure rise time was set at 0 secs, and the PSV cycling-off criterion was 25% of peak flow.

To ensure that PSV and PAV provided an equivalent level of support, we provided an equal degree of respiratory muscle unloading for both PSV and PAV relative to spontaneous breathing (SB) (18). The pressure time product (PTP) per minute of the respiratory muscles was the target variable (18). Briefly, baseline mechanical ventilation was discontinued, and the patient was allowed to breathe spontaneously for 3 mins; flow and airway (Pao) and esophageal (Pes) pressure tracings were collected. PTP per breath (PTP/b) was obtained by measuring the area under Pes from the beginning of the inspiratory deflection to the end of inspiratory flow (18). PTP/min was calculated as PTP/b multiplied by respiratory rate (18). Transpulmonary pressure was obtained by subtracting Pes from Pao. Resistance (R_L) and elastance (E_L) were calculated using the Mead and Wittenberger technique (19). All variables were determined as mean values of the 3 mins of SB. Approximately 20–30 mins after these measurements, during PSV we set the level of pressure to obtain a 50% decrease in PTP/min relative to the values obtained during SB. Values of R_L and E_L obtained during SB were used to set PAV; resistive and elastic proportionality factors were set at levels equal to 50% of R_L and E_L, respectively, and then adjusted to obtain a PTP/min equal to 50% of the value obtained during SB (19).

All data were recorded from 10:00 pm to 8:00 am for the two consecutive study nights.

Table 1. Patient characteristics

Patient No.	Gender	Age, Yrs	Diagnosis	SAPS II	Days on MV Prior to Study, No.	Days on MV After Study, No.	pH	$Paco_2$, mm Hg	Pao_2/Fio_2
1	M	52	Pneumonia	36	20	4	7.44	41.6	297
2	M	67	Myasthenia gravis	33	31	3	7.43	44.0	304
3	M	74	Sepsis	47	38	27	7.46	35.5	266
4	F	77	Sepsis	47	35	4	7.45	43.7	306
5	M	75	ARDS	47	24	4	7.47	47.3	354
6	M	60	Pneumonia	32	24	11	7.4	45.0	256
7	M	58	ARDS	26	9	9	7.47	41.8	303
8	M	59	Sepsis	45	7	6	7.44	30.4	376
9	M	72	Multiple trauma	38	24	3	7.45	38.4	340
10	F	69	Pneumonia	39	18	7	7.42	51.7	299
11	M	65	Pneumonia	37	15	4	7.47	32.8	318
12	F	28	ARDS	30	31	3	7.45	37.3	360
13	M	63	Pneumonia	32	5	6	7.42	43.4	207
Mean		63		38	22	7	7.44	40	307
SD		13		7	11	6	0.02	6	46

SAPS, Simplified Acute Physiology Score; MV, mechanical ventilation; ARDS, acute respiratory distress syndrome.

Data acquisition was continuously attended to ensure quality of all tracings.

Sleep was recorded using standard polysomnography (Sandman, NPB-Mallinckrodt, Minneapolis, MN). All polysomnography records were scored manually by an expert (AB) blinded to respiratory signals (20). Arousals and awakenings were identified as electroencephalographic activations lasting 3–15 secs and >15 secs, respectively (21). Arousals caused by noise were identified as electroencephalographic activations occurring during or within 3 secs of completion of a noise increase of >10 dB (21). Sleep quantity was estimated as sleep efficiency and sleep maintenance efficiency (21).

A luxometer and a microphone measured light and noise intensity at the bedside (KleisTEK Advanced Electronic Systems, Bari, Italy). Light intensity was measured in lux and noise in decibels, analyzed as the mean and maximum levels occurring per 10-min interval, and expressed as the average value for the entire night (22, 23). The number of noise peaks >75 dB was counted every 10-min interval and expressed as the total number for the entire night (23).

Flow, Pao, Pes, and end-tidal CO_2 were measured and recorded (ICU-Lab, KleisTEK Engineering, Bari, Italy) (18, 19, 24). Arterial blood gases were measured at the beginning and the end of the data recording. The 10-hr recording for each night was divided into 1-min segments; 1 min every 20 mins was analyzed for each night on a breath-by-breath basis. Inspiratory time, expiratory time, total breathing cycle time, tidal volume (V_T), minute ventilation (V_E), and intrinsic PEEP were measured as previously described (19).

Patient respiratory rate (number of Pes deflections occurring in 1 min) and ventilator respiratory rate (number of flow inflections occurring in 1 min) were calculated per 1-min segment randomly selected every 10 mins. Breath-by-breath analysis was performed in all segments that showed a difference between patient and ventilator respiratory rates. Patient-ventilator asynchronies were identified as a) auto-triggering, ventilator-delivered breaths occurring in the absence of an inspiratory effort; b) ineffective triggering, inspiratory efforts that failed to trigger a ventilator-assisted breath; c) double triggering, the ventilator providing two pressure boosts for a single inspiratory effort; and d) delayed cycling, the ventilator providing a single pressure boost that spanned two inspiratory efforts (19). Central apneas were defined as an absence of flow and inspiratory effort lasting ≥10 secs and expressed as the total number of apneas per night (9).

To determine the relative proportion between ventilator-delivered pressure and patient inspiratory effort, the ratio between the area under the Pao (PTP/b_{Pao}) and Pes (PTP/b_{Pes}) tracing (from the beginning of the inspiratory deflection to the end of inspiratory flow) was calculated (19).

Results are reported as mean ± SD or median and range and compared using paired Student's *t*-test or Wilcoxon's signed-rank test when appropriate. Multivariate analysis of variance was used to evaluate the effect of mode of ventilation on comprehensive sleep quality (9, 16, 22, 23). Simple linear regression analysis was performed to determine the relationship between arousals and patient-ventilator asynchrony. A probability of .05 on two-sided testing was regarded as being significant (SPSS 13.0, Chicago, IL).

RESULTS

Sixteen patients met enrollment criteria; three patients were withdrawn because of sepsis (two patients) and severe hypoxemia (one patient) (Fig. 1). All patients achieved sleep and had physiologic tracings that could be analyzed; 9–11 hrs of sleep recordings and 1400–1500 breaths were therefore analyzed for each patient every study night.

Table 2. Respiratory mechanics during the spontaneous breathing trial preceding proportional assist ventilation (PAV) and pressure support ventilation (PSV)

Respiratory Variable	PAV	PSV
PTP/min, cm H_2O·sec/min	371 ± 201	398 ± 203
R_L, cm H_2O/L/sec	10.4 ± 6.6	11.1 ± 4.6
E_L, cm H_2O/L	22.6 ± 11.7	21.3 ± 10.9
$PEEP_i$, cm H_2O	2.9 ± 1.1	3.2 ± 1.8

PTP/min, pressure time product per minute; R_L, dynamic lung resistance; E_L, dynamic lung elastance; PEEPi, intrinsic positive end-expiratory pressure. *p* value is nonsignificant for all paired comparisons.

Characteristics of the study population are provided in Table 1. All patients were successfully weaned from mechanical ventilation and discharged alive from the ICU. Before study enrollment, six patients were sedated with lorazepam (0.007 ± 0.01 mg/kg/hr) and seven patients with propofol (0.09 ± 0.04 mg/kg/hr). Treatment with lorazepam and propofol was interrupted 8 ± 5 days and 4 ± 2 days before study entry, respectively. During the study, patients 6, 7, and 8 required morphine (average dose 0.008 ± 0.002 mg/kg/hr) and patients 7 and 8 required haloperidol (4 and 8 mg/24 hr, respectively); doses of medications were not changed during the two study nights. No patient received antidepressant medication during the study period.

PTP/min, R_L, E_L, and intrinsic PEEP during the SB trial preceding PSV and PAV are provided in Table 2. On PSV, 9.2 ± 2.8

Table 3. Arterial blood gases 1 hr after onset of sleep study (10 am)

Arterial Blood Gas	PAV	PSV
Pa_{O_2}, mm Hg	109 ± 27	105 ± 19
Pa_{CO_2}, mm Hg	41 ± 6	40 ± 6
pH	7.45 ± 0.01	7.44 ± 0.02

PAV, proportional assist ventilation; PSV, pressure support ventilation.
$p < .05$.

Table 4. Respiratory variables during proportional assist ventilation (PAV) and pressure support ventilation (PSV)

Respiratory Variable	PAV	PSV
V_T, L[a]	0.59 ± 0.13	0.63 ± 0.13[b]
Ti/Ttot, %[a]	41 ± 5	40 ± 3
RR, breaths/min[a]	24.5 ± 6.1	24.2 ± 5.3
V_E, L/min[a]	13.5 ± 2.3	14.4 ± 2.7[b]
$Petco_2$, mm Hg[a]	39.4 ± 6.8	37.3 ± 5.3[b]
pH[c]	7.43 ± 0.03	7.44 ± 0.03
Morning Pa_{O_2}, mm Hg[c]	112 ± 15	109 ± 22
Morning $Paco_2$, mm Hg[c]	43 ± 4	41 ± 4[b]
Pao, cm H_2O	11.7 ± 3.5	13.3 ± 3.2[b]
PTP/min, cm H_2O·sec/min	197 ± 78	174 ± 56

V_T, tidal volume; Ti, inspiratory time; Ttot, respiratory duty cycle; RR, respiratory rate; V_E, minute ventilation; $Petco_2$: end-tidal CO_2; Pao, airway opening pressure; PTP/min, pressure time product per minute.
[a]Average values of the study night; [b]$p < .05$; [c]values obtained at 8:00 am after study conclusion.

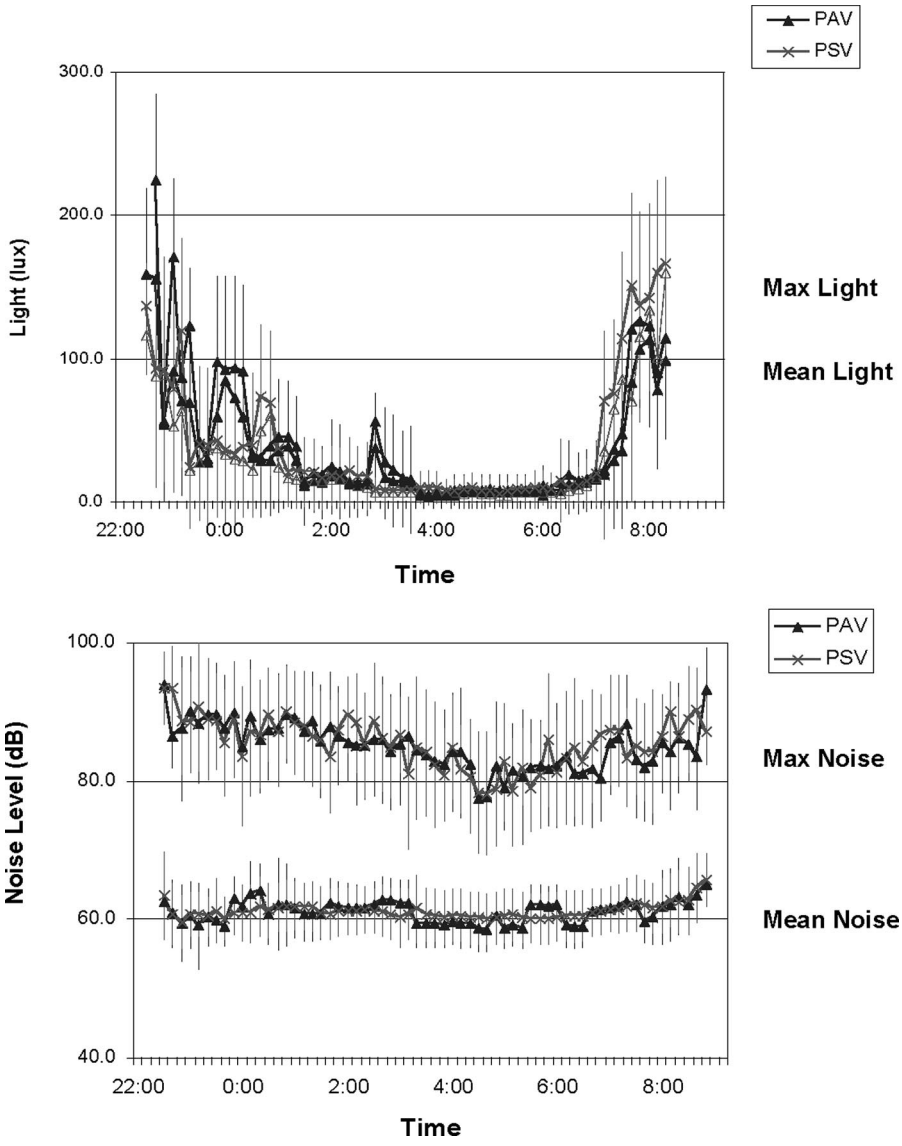

Figure 2. Environmental light and noise. Maximum and mean light intensity (*top*) and noise levels (*bottom*) measured in 10-min intervals during the nights on pressure support ventilation (*PSV*) and proportional assist ventilation (*PAV*).

cm H_2O of ventilator-applied pressure was required to achieve a 54 ± 3% reduction in the inspiratory muscle load relative to spontaneous breathing. On PAV, the 53 ± 5% reduction of the PTP/min was obtained by setting the flow assistance to 5.8 ± 2.9 cm H_2O/L/sec (54 ± 14% of R_L) and the volume assistance to 8.9 ± 2.6 cm H_2O/L (60 ± 16% of E_L). PEEP and FIO_2 were set equivalently in both modes at 5.5 ± 0.2 cm H_2O and 37 ± 5%, respectively.

Initial monitoring of ventilatory variables for PSV and PAV during wakefulness revealed no significant differences in inspiratory muscle effort, V_T, or respiratory rate, with average values of 186 ± 100 cm H_2O·sec/min, 0.59 ± 0.12 L, and 26 ± 6, respectively. At the beginning of the study nights, baseline values of Pa_{O_2}, $Paco_2$, and arterial pH did not differ between PAV and PSV (Table 3).

Mean values of PTP/min during the study nights did not differ between PSV and PAV. However, Pao, V_T, and V_E were 7 ± 1, 19 ± 3, and 7 ± 2% higher during PSV than during PAV, respectively ($p < .05$). Consequently, mean values of end-tidal CO_2 for the entire study night and morning $Paco_2$ values were significantly ($p < .05$) lower during PSV than during PAV (Table 4).

Figure 2 shows that maximum and mean environmental noise and light did not differ between PSV and PAV; the number of noise peaks >75 dB was 942 ± 293 during PSV and 883 ± 275 during PAV.

Arousals per hour of total sleep time were 16 (range 2–74) during PSV and 9 (range 1–41) during PAV ($p < .02$). Arousals per hour caused by noise were 2 (0–17) on PAV and 2 (0–16) on PSV. Multivariate analysis of variance showed that overall sleep quality was significantly improved on PAV ($p < .05$) due to the combined effect of fewer arousals per hour, fewer awakenings per hour (3.5 [0–24] vs. 5.5 [1–24]), and greater rapid eye movement (9% [0–31] vs. 4% [0–23]) and slow wave (3% [0–16] vs. 1% [0–10]) sleep (Fig. 3), although individual sleep stages were not significantly different between modes. Quantity of sleep was equivalent with PSV and PAV (Table 5).

Episodes of central apnea were observed in patients 2 and 8 during the night on PSV (17 and 14 apneas per night, respectively), whereas no patients showed central apneas during the night on PAV. No significant desaturations

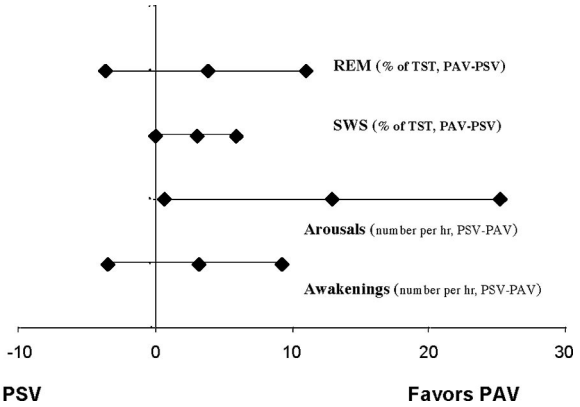

Figure 3. Multivariate analysis of variance of the effect of modes of ventilation on comprehensive sleep quality. Central diamond indicates the mean absolute difference between proportional assist ventilation (*PAV*) and pressure support ventilation (*PSV*); horizontal bar indicates the 95% confidence interval. The combined effect of fewer arousals per hour, fewer awakenings per hour, greater rapid eye movement (*REM*) sleep, and greater slow wave sleep (*SWS*) accounted for the significant ($p < .05$) overall improvement in sleep quality with PAV. *TST*, total sleep time.

Table 5. Sleep quantity during the nights on proportional assist ventilation (PAV) and pressure support ventilation (PSV)

Sleep Variable	PAV	PSV
TST, min	334 ± 124	314 ± 140
TSP, min	451 ± 99	484 ± 63
SE, %	60 ± 23	58 ± 25
SME, %	69 ± 22	68 ± 21

TST, total sleep time; TSP, total sleep period; SE, sleep efficiency; SME, sleep maintenance efficiency.

Table 6. Patient-ventilator asynchrony

Type of Asynchrony	PAV	PSV
Auto-triggering	5.4 ± 8.2	25.8 ± 42.3[a]
Ineffective triggering	11.6 ± 10.8	19.6 ± 31.8
Double triggering	5.8 ± 7.3	7.3 ± 6.8
Delayed cycling	0.6 ± 1.0	3.1 ± 4.6[a]
Total asynchronies	23.7 ± 15.4	52.9 ± 59.2[a]

PAV, proportional assist ventilation; PSV, pressure support ventilation.

[a]$p < .05$. All values are n/hr.

were observed during the apneas. Neither patient with central apnea had congestive heart failure; patient 8 received a low-dose morphine infusion at 0.005 mg/kg/hr during both study nights.

Table 6 provides frequencies of patient-ventilator asynchronies on PAV and PSV. Total patient-ventilator asynchronies per hour were more frequent during PSV than during PAV and correlated significantly with the number of arousals per hour ($R^2 = .65$, $p = .0001$) (Fig. 4, *left*). The $PTP/b_{Pao}/PTP/b_{Pes}$ ratio correlated significantly with the number of arousals per hour ($R^2 = .71$, $p = .0001$) (Fig. 4, *center*). The number of patient-ventilator asynchronies was correlated to $PTP/b_{Pao}/PTP/b_{Pes}$ regardless of the ventilatory mode ($R^2 = .52$, $p = .0001$) (Fig. 4, *right*).

DISCUSSION

Sleep disruption is common in the critically ill (4, 25, 26) and may influence clinical course due to its effect on metabolism (27), respiratory muscle endurance (28), delirium (26, 29), immunity (30), and outcome of mechanical ventilation (31). Although quantity of sleep was unchanged, we observed better quality of sleep on PAV, with overall improvement in sleep architecture and reduced sleep fragmentation.

A key element of the study was to provide equivalent levels of support during PSV and PAV. This was achieved by setting the level of pressure (during PSV) and the resistive and elastic proportionality factors (during PAV) to obtain a similar amount of respiratory muscle unloading relative to an SB trial. Although this approach for setting ventilatory support does not represent standard clinical practice, it was required to ensure a meaningful comparison between PSV and PAV (32). Optimal patient-ventilator interactions explain the observed improvement in sleep quality since effects of sedative and analgesic medications were minimized by selecting patients who were receiving only low-dose morphine infusions at equivalent rates during both study nights and by withdrawing sedative agents ≥36–72 hrs before sleep measurement. Moreover, biases due to severity of illness or acclimatization to study equipment were minimized by the randomized crossover study design. Although interruptions caused by increased noise or light may have contributed to sleep disruption, environmental conditions were equivalent during both nights and therefore do not explain the observed difference in sleep quality between the two modes.

At any instant during a breath, the pressure applied to the patient's respiratory system includes the pressure generated by the respiratory muscles and the pressure delivered by the ventilator (33). Patient-ventilator interactions are therefore determined by a) the synchrony between the timing of the patient effort and the ventilator-delivered breath; and b) the agreement between the magnitude of patient inspiratory effort and the amount of ventilatory support (33). Our data show that the occurrence of asynchrony significantly correlated to the proportion between ventilator-applied and patient-generated pressures ($R^2 = .52$, $p = .0001$) (Fig. 4, *right*). Patient-ventilator asynchronies per hour correlated significantly with the number of arousals per hour ($R^2 = .71$, $p = .0001$) (Fig. 4, *left*). The improvement in all variables of sleep quality with PAV could therefore be attributed to the reduction in patient-ventilator asynchronies. However, when PSV settings led to a small number of asynchronies, indicators of sleep quality were similar to those observed on PAV.

The proportion between PTP/b_{Pao} and PTP/b_{Pes} correlated with the number of arousals ($R^2 = .71$, $p = .0001$) (Fig. 4, *center*). On PAV, in eight patients the $PTP/b_{Pao}/PTP/b_{Pes}$ ratio ranged from 0.5 and 0.7; in these patients arousals per hour were 7 ± 3. In the remaining five patients, the $PTP/b_{Pao}/PTP/b_{Pes}$ ratio ranged between 1.0 and 1.7; in these patients arousals per hour were 22 ± 12. On PSV, in nine patients $PTP/b_{Pao}/PTP/b_{Pes}$ ratio ranged between 1 and 5; in these patients arousals per hour were 34 ± 23. In the remaining four patients the $PTP/b_{Pao}/PTP/b_{Pes}$ ratio ranged between 0.5 and 0.8 and arousals per hour were 7 ± 5. These data suggest that synchrony between ventilator timing and breathing pattern and balance between patient-generated and ventilator-delivered pressure influence quality of sleep regardless of ventilatory mode. Although

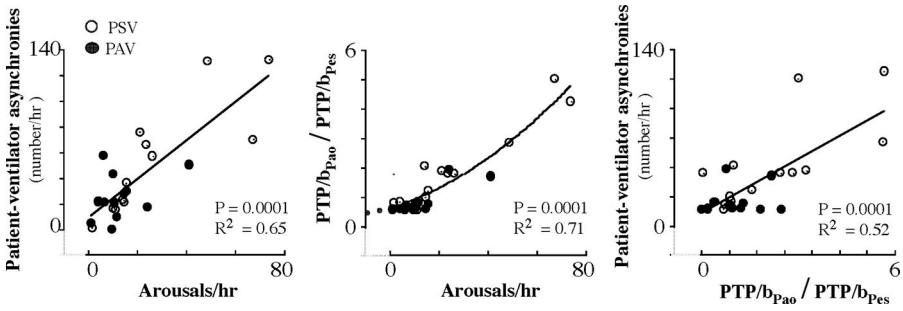

Figure 4. Simple linear regression analysis correlating the number of patient-ventilator asynchronies per hour with the $PTP/b_{Pao}/PTP/b_{Pes}$ (*right*), the number of patient-ventilator asynchronies per hour with the number of arousals per hour (*left*), and the $PTP/b_{Pao}/PTP/b_{Pes}$ ratio with the number of arousals per hour (*center*). *Open circles*, pressure support ventilation (*PSV*); filled circles, proportional assist ventilation (*PAV*). *PTP/b*, pressure time product per breath; *Pao*, airway opening pressure; *Pes*, esophageal pressure.

PAV enhances the ventilator's ability to match patient ventilatory needs, setting PSV based on measurements of a patient's inspiratory effort may optimize patient-ventilator interaction and minimize sleep fragmentation (10). On PSV, patient-ventilator asynchronies could be further reduced by tailoring the trigger sensitivity, rise time, and cycling-off criteria to suit the respiratory mechanics and breathing pattern of the individual patient and then adjusting these variables as necessary to compensate for changes during sleep and wakefulness (10). Conversely, PAV should obviate the need to continuously adjust ventilator settings since ventilator-applied pressure rises and falls according to the contour of the patient's effort and changes proportionally to changes in inspiratory effort (10).

Parthasarathy and Tobin (9) demonstrated that six of 11 patients developed apneas when PSV was set to obtain a target VT of 8 mL/kg. In our study, during PSV, a Pao of 9.2 ± 2.8 cm H_2O and a VT of 0.63 ± 0.13 L (6.6 ± 0.2 mL/kg) were required to achieve the target value of a 54 ± 3% reduction in the inspiratory muscle load (relative to the inspiratory muscle load measured during an SB trial). On these settings, episodes of central apnea occurred in only two of 13 patients. These data confirm Fanfulla and coworkers' (10) findings that setting PSV based on measurements of a patient's inspiratory effort may reduce apneas and sleep fragmentation, compared with routine settings based on clinical variables such as patient respiratory rate or VT. Furthermore, setting PAV to reduce the inspiratory muscle effort by 53 ± 5% completely prevented central apneas in the same patient group.

During normal sleep, down-regulation of the respiratory muscles occurs, resulting in a decrease in VE and concordant increase in CO_2. Since PSV operates based on preset target levels for pressure and cycling-off criteria, a patient's ability to modulate ventilator-delivered assistance on PSV is limited (32). When patients' ventilatory requirements or breathing patterns change, as they do naturally during sleep, PSV settings that were appropriate while awake may result in delivery of excessive VE, leading to periodic breathing or apneas (32). Conversely, PAV links both the level and timing of ventilator assistance to the magnitude and time course of patient effort. Because there is no preset target level for either pressure flow or volume, PAV responds more optimally to the down-regulation of respiratory muscles during sleep (32), which leads to lower ventilator assistance than on PSV (33). Confirming these theoretical advantages, we observed that ventilator-delivered pressure and volume for a given inspiratory effort were lower during PAV than during PSV. PAV therefore preserved the physiologic increase in $Paco_2$ during sleep (34) and prevented any patient from developing central apneas, thereby reducing sleep fragmentation.

Prevention of central apneas is only one of the means to reduce sleep disruption in critically ill patients. Parthasarathy and Tobin (9) showed that apnea-related sleep fragmentation was significantly reduced by adding deadspace to the ventilator circuit or by setting a back-up rate using assist control ventilation. However, in Parthasarathy and Tobin's study, all other non-apnea-related arousals and awakenings were equally frequent during PSV and assist-control ventilation. In the present study, PAV also reduced the non-apnea-related arousals (12.8 ± 10.2 vs. 23.2 ± 22.8 arousals per hour during PAV and PSV, respectively; $p < .05$), indicating that factors other than apnea prevention contributed to the improvement in sleep quality.

CONCLUSIONS

This study confirms the hypothesis that patient-ventilator discordance may cause sleep disruption and highlights potential means of improving sleep quality in the ICU through careful selection of ventilator settings. Although during PSV patient-ventilator asynchrony and apneas could be minimized by setting the level of ventilatory support in accordance with inspiratory muscle effort, PAV was more efficacious in matching changes in patient ventilatory requirements and breathing pattern with ventilator-delivered assistance, therefore resulting in fewer patient-ventilator asynchronies and better quality of sleep.

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