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Partitioning of inhaled ventilation between the nasal and oral routes during sleep in normal subjects

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Fitzpatrick, Michael F., Helen S. Driver, Neela Chatha, Nha Voduc, and Alison M. Girard. Partitioning of inhaled ventilation between the nasal and oral routes during sleep in normal subjects. *J Appl Physiol* 94: 883–890, 2003. First published November 1, 2002; 10.1152/japplphysiol.00658.2002.—The oral and nasal contributions to inhaled ventilation were simultaneously quantified during sleep in 10 healthy subjects (5 men, 5 women) aged 43 ± 5 yr, with normal nasal resistance (mean 2.0 ± 0.3 $cmH_2O \cdot l^{-1} \cdot s^{-1}$) by use of a divided oral and nasal mask. Minute ventilation awake (5.9 ± 0.3 l/min) was higher than that during sleep (5.2 ± 0.3 l/min; $P < 0.0001$), but there was no significant difference in minute ventilation between different sleep stages ($P = 0.44$): stage 2 5.3 ± 0.3, slow-wave 5.2 ± 0.2, and rapid-eye-movement sleep 5.2 ± 0.2 l/min. The oral fraction of inhaled ventilation during wakefulness (7.6 ± 4%) was not significantly different from that during sleep (4.3 ± 2%; mean difference 3.3%, 95% confidence interval −2.1–8.8%, $P = 0.19$), and no significant difference ($P = 0.14$) in oral fraction was observed between different sleep stages: stage two 5.1 ± 2.8, slow-wave 4.2 ± 1.8, rapid-eye-movement 3.1 ± 1.7%. Thus the inhaled oral fraction in normal subjects is small and does not change significantly with sleep stage.

upper airway; control of breathing; sleep apnea; oronasal

ALTHOUGH MUCH IS KNOWN ABOUT respiration during sleep, it is remarkable that the partitioning of inhaled ventilation between the oral and nasal routes during sleep in healthy humans with normal nasal resistance has not been described. In particular, although it is widely assumed that inhalation takes place via the nasal route throughout all sleep stages, there have been no objective measurements of inhaled oral ventilation during sleep to support this assumption. A description of the inhaled breathing route during sleep is an important step in understanding normal upper airway physiology during sleep and may provide an important reference point for assessment of patients with disease.

It is conceivable that oral-nasal partitioning of inhaled ventilation could change with different stages of sleep or with position. For example, snoring was reported to be louder during slow wave and rapid-eye-movement (REM) sleep than other sleep stages (11). In addition, the primary site responsible for generating the snore vibration, which can originate from the soft palate or from the tongue base (30), may vary during the night (10). In patients with obstructive sleep apnea (OSA), one study demonstrated a change in the primary site of upper airway obstruction with sleep stage, from the velopharyngeal level in non-REM sleep to the hypopharyngeal level during REM sleep (4).

The advent of the nasal cannula pressure transducer as the preferred device for airflow measurement during sleep, because of its higher sensitivity for detection of airflow limitation (27), is also predicated on the assumption that airflow during sleep is primarily via the nasal route, regardless of sleep stage. Indeed, not all commercial nasal cannula pressure transducer devices include a sensor for oral airflow.

Limited available evidence suggests that more of the exhaled minute ventilation occurs through the oral route in snorers and patients with OSA than is the case in normal subjects (9). Jaw opening was observed to increase at end inspiration, compared with end expiration, in both normal subjects and patients with OSA, but, at both points in the breathing cycle, jaw opening was greater in patients with OSA than in normal subjects (12). Oral-nasal partitioning of inhaled ventilation is an important aspect of respiratory physiology during sleep to understand, because there is quite consistent literature demonstrating an increased tendency to OSA with nasal obstruction (and presumably increased mouth breathing). In particular, because nasal resistance varies considerably from time to time in normal subjects but is a major determinant of mouth breathing (18, 33) and is higher among snorers and patients with OSA (26, 19), it is important to document the nasal resistance when describing the breathing route during sleep in normal subjects.

We hypothesized that, once subjects were asleep, the oral fraction of inhaled ventilation would vary with sleep stage; this hypothesis was based on the rather preliminary evidence mentioned above, that snoring volume and the site of upper airway obstruction may change with sleep stage. This study was undertaken to test that hypothesis and to describe nasal and oral

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partitioning of inhaled ventilation during sleep in a group of healthy subjects with normal nasal resistance.

MATERIALS AND METHODS

Ten subjects (5 men, 5 women) were studied (Table 1). Subjects were recruited by newspaper advertisement and screened by questionnaire, spirometry, and acoustic rhinometry to exclude those with *1*) upper or lower respiratory tract disease, including any history of nasal allergy; *2*) current respiratory tract infection; *3*) known sleep disorders (sleep apnea, insomnia, irregular sleep-wake cycle); *4*) a history of regular loud snoring; *5*) moderate or severe obesity (body mass index $>$ 30); *6*) claustrophobia; *7*) current or recent (within 2 yr) cigarette smoking; and *8*) those currently taking medication. All patients had normal spirometry and flow volume contours: mean forced expiratory volume in 1 s (% predicted) 112 ± 19, range 82 −140%; mean forced vital capacity (%predicted) 104 ± 15, range 85–131%. Within 2 wk of the screening measurements being performed, subjects were scheduled to return for measurement of nasal resistance and for overnight polysomnography, including simultaneous measurement of oral and nasal inhaled ventilation. Subjects were asked to refrain from caffeine for 12 h before the overnight study and to avoid any naps during the 12 h before study.

Nasal resistance was measured in the erect seated position, by posterior active rhinomanometry, 2 h before the start of the overnight sleep study. An infant nasogastric feeding catheter (6-Fr diameter-MED-Rx Benlan, Oakville, Ontario, Canada) was lubricated and inserted through the right nostril until it was visible at the pharynx on mouth opening. The distal catheter tip was then retracted 1.5 cm above the free margin of the soft palate. The proximal end of the cannula was attached to a differential pressure transducer (Ultima dual-pressure sensor, model 0585; Braebon Medical, Kanata, Ontario, Canada), which was calibrated to ±4 V = ±20 cmH_2O. A continuous positive airway pressure (CPAP) mask was placed over the patient's nose, taking care to ensure that there was no compression of the nasal airway by the mask (by monitoring the posterior nasal pressure before and after attachment of the nasal mask) and ensuring that there was no air leak from the mask. A heated pneumotach (3700 series, Hans Rudolph, Kansas City, MO) was placed at the outlet of the CPAP mask, and the patient was instructed to breathe quietly through the nose only, with the lips closed. An identical catheter to that used for measurement of posterior nasal pressure was employed to measure pressure at the anterior nares (this provided the reference pressure for calculation of the differential pressure across the nasal airway). This tube was passed through a port in the CPAP mask, the port was then made airtight by using adhesive, and the proximal end of the catheter was attached to the differential pressure transducer. Each pneumotach was calibrated with a 3-liter syringe to an accuracy of ±0.5% before each study. Nasal resistance was measured as the change in pressure (cmH_2O) across the nose for a standardized inspiratory flow rate of 0.3 l/s (9).

Sleep recordings. Each subject underwent overnight polysomnography at the Sleep Laboratory, Kingston General Hospital. Sleep recordings were similar to the routine clinical polysomnogram [4 EEG channels (C4–A1, C3–A2, O2–A1, O1–A2); 2 electrooculogram channels (ROC-A1, LOC-A2); submental electromyogram (EMG); intercostal (diaphragmatic surface) EMG; ECG; chest and abdominal movement; piezo bands; finger pulse oximetry; bilateral anterior tibialis EMG, vibration snore sensor] except for the measurements of oral and nasal ventilation (see *Simutaneous measurement of oral and nasal ventilation during sleep studies*). The sleep data were collected and scored by use of "Sandman" software [Mallinckrodt, Nellcor Puritan Bennett (Melville), Ottawa, Ontario, Canada]. The overnight sleep recordings were conducted from 11 PM until 7 AM, continuously or until the subject requested that the study be terminated. Data for one full epoch (30 s) of continuous sleep, or until tidal volume stabilized for three consecutive breaths during sleep, before and after spontaneous arousals, were excluded from analysis. Because physiological central hypopneas and apneas are known to occur during phasic REM sleep, data surrounding (30 s of continuous sleep before and after) respiratory events associated with cortical arousals were excluded from REM sleep analysis.

Simultaneous measurement of oral and nasal ventilation during sleep studies. Subjects wore a molded single-piece translucent silicone rubber mask (7900 series mask, Hans Rudolph), with a built-in partition separating the oral and nasal ports. An identical heated pneumotach (3700 series, flow 0–160 l/min, Hans Rudolph) was inserted in each of the two mask ports (oral and nasal) to measure nasal and oral ventilation separately. Each of the two pneumotachs was connected to a corresponding RSS100HR research pneumotach system (Hans Rudolph). The digital outputs from the RSS100HR system (proximal port pressure, flow, tidal volume) were interfaced with the computerized polysomnographic montage to permit simultaneous recognition of the

Table 1. *Demographics and lung function for the 10 normal subjects studied*

Subjects	Gender	Age, y	Height, m	Weight, kg	BMI, kg/m^2	FEV_1, liters	FEV_1, %pred	FVC, liters	FVC, %pred
1	M	63	1.73	70	23.2	4.27	143	5.58	131
2	M	43	1.80	85	26.2	3.97	132	4.64	123
3	M	28	1.80	80	24.7	4.94	113	6.06	109
4	M	51	1.80	84	25.0	3.47	82	4.47	93
5	M	53	1.70	81	28.0	3.08	95	3.73	85
6	F	39	1.64	58	21.6	3.01	91	3.81	97
7	F	24	1.63	61	23.0	3.56	129	3.97	112
8	F	22	1.68	61	21.6	4.03	117	4.15	97
9	F	41	1.63	61	23.0	3.56	129	3.97	112
10	F	68	1.62	68	25.9	2.30	113	2.77	97
Mean		43	1.70	70.5	24.1	3.60	112	4.29	104
SD		16	0.10	11	2.2	0.74	19	0.96	15

M, male; F, female; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; %pred, percent of predicted value; FVC, forced vital capacity.

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sleep stage, oral and nasal airflow, and oral and nasal tidal volumes (Fig. 1). The seal on the oronasal mask was checked in the following ways: *1*) visually inspecting and palpating to ensure that there was no air leak discernible to the subject or investigators; *2*) attaching a CPAP unit (KnightStar, KnightStar, Tyco Healthcare Nellcor Puritan Bennett, Mallinckrodt) at 4-cmH_2O pressure output (flow rate through pneumotach 98 l/min) to each port of the face mask, separately, while ensuring that the CPAP leak display remained at zero and that there was no discernible air leak on careful mask inspection and palpation; *3*) asking the patient to hold breath with the CPAP unit at 4 cmH_2O attached to the oral pneumotach and then recording any air flow through the nasal pneumotach (this tested for any leak between the oral and nasal compartments of the mask), and vice versa; and *4*) asking the patient to breathe through the mouth only and checking for any detectable flow through the nasal pneumotach, and vice versa. End-tidal CO_2 monitoring was explored as a method of measuring mask leak but was abandoned when it became obvious that it was insensitive to small mask leaks that were evident by using the other techniques. Assessments for a mask leak were repeated at lights out, at lights on, and during periods of sustained wakefulness during the night. Theatrical spirit gum (Graftobian, Madison, WI) was used to seal the contact between the oronasal mask and skin. The dead space of the oronasal mask (no. 7920, adult large) was 31.3 ml. The dead space of each of the two pneumotachs was 13.87 ml. Hence, the total dead space of the experimental setup was 59 ml. The resistance of each pneumotach was identical (0.019 $cmH_2O \cdot l^{-1} \cdot min$ at a flow rate of 16 l/min).

Analysis of oral and nasal tidal volumes was done manually, breath by breath, from the computer screen by placing a cursor over the maximum point on the oral and nasal tidal volume curves, reading the corresponding volume from the voltmeter display, and subtracting the baseline volume. All eligible breaths for every epoch of sleep and quiet wakefulness were analyzed in each subject.

Statistical analysis. Repeated-measures ANOVA was used to test for differences in mean values during different sleep stages (the residuals were plotted to ensure constant variance and normality). Two-way ANOVA was used to analyze the effects of posture and gender on ventilatory parameters during sleep. Paired *t*-testing was used to examine intraindividual differences between pooled values during wakefulness and sleep.

RESULTS

All subjects had nasal resistance values that were within normal limits (mean 2.0 ± 0.3, range 1.0–3.0 $cmH_2O \cdot l^{-1} \cdot s$) immediately preceding overnight polysomnography. The sleep stage information obtained during overnight polysomnography for each subject is displayed in Table 2. The mean sleep duration was 4 h (239.3 ± 17.2 min), and the mean sleep efficiency was

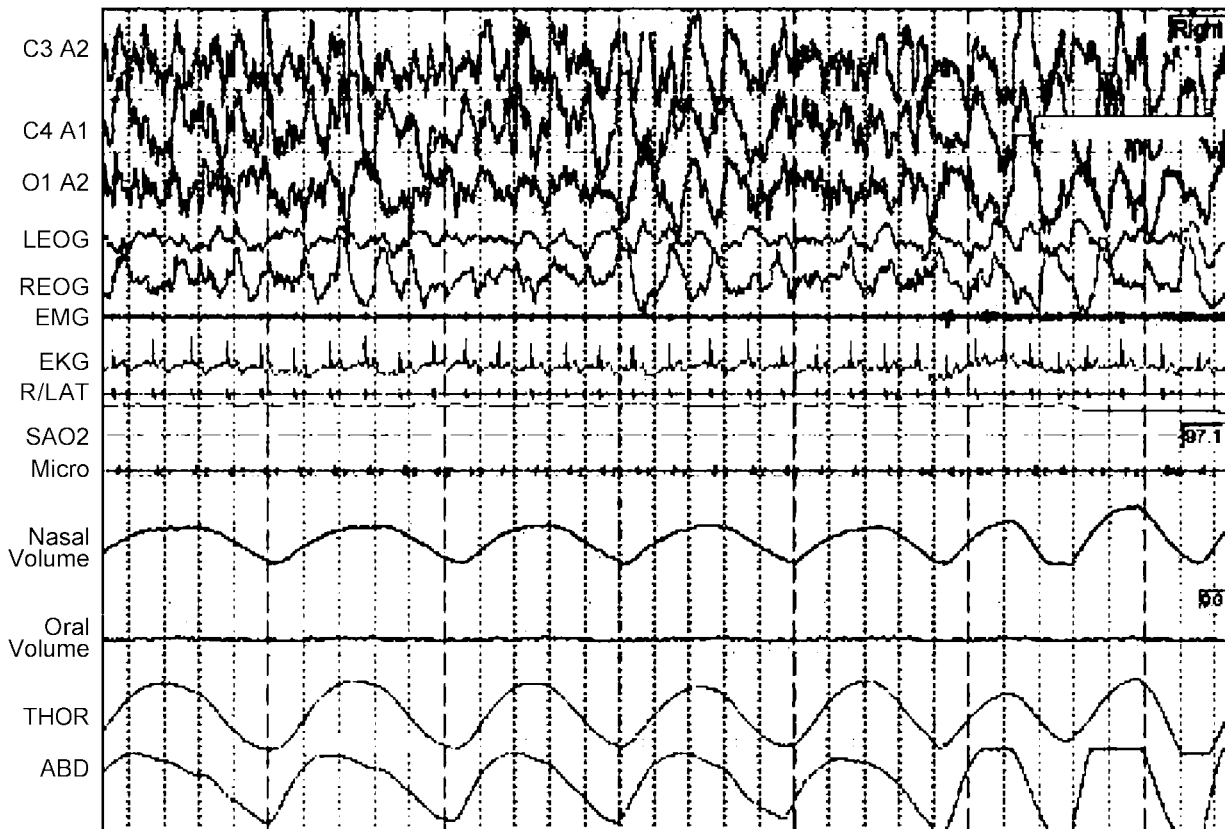

Fig. 1. A 30-s epoch of raw data demonstrating almost exclusive nasal ventilation in a normal subject during slow-wave sleep and during a subsequent spontaneous arousal. C3 A2, C4 A1, and O1 A2, 2 central and 1 occipital EEG, respectively; LEOG and REOG, left and right electrooculogram, respectively; EMG, submental electromyogram; EKG, electrocardiogram; R/LAT, right and left anterior tibialis EMG; SAO2, oxygen saturation tracing; Micro, snore vibration sensor; Nasal and Oral Volume, breath-by-breath tracing of nasal and oral tidal volume, respectively; Thor and ABD, chest wall and abdominal movement with respiration, respectively.

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Table 2. *Objective sleep data for 10 normal subjects sleeping with the oronasal mask and pneumotach system*

Subject	TRT, min	SOL, min	REML, min	Awake, min	TST, min	1, %	2, %	SWS, %	REM, %	SEFF, %	Supine, %
1	315	8	85	115	192	17	64	12	8	61	37
2	324	2	117	114	209	8	55	15	22	64	7
3	377	10	170	59	307	9	62	10	19	82	54
4	311	69	140	77	165	31	58	6	6	53	28
5	416	7	84	190	219	20	57	4	19	53	22
6	334	15	199	54	266	19	61	11	8	80	65
7	278	9	72	22	247	12	38	33	17	89	52
8	390	17	207	190	183	24	52	16	8	47	25
9	333	5	68	43	285	23	53	12	13	85	8
10	417	16	173	79	323	20	44	11	22	77	21

TRT, total recording time; SOL, sleep onset latency; REML, rapid eye movement (REM) latency; Awake, time spent awake; TST, total sleep time; 1, %sleep stage 1; 2, %sleep stage 2; SWS, %stages 3 and 4; REM, %REM sleep; SEFF, sleep efficiency [(TST × 100)/TRT]; Supine, %total sleep time in supine position.

69 ± 5%. Despite wearing the somewhat cumbersome sealed oronasal mask system, each of the 10 subjects had adequate amounts of all sleep stages without arousals, including REM and slow-wave (stages 3 and 4) sleep, to permit characterization of oral and nasal ventilation for that person in that sleep stage. The total sleep time for all 10 subjects was broken down as follows: stage 1, 17 ± 2; stage 2, 49.4 ± 3; stages 3 and 4, 13 ± 2; REM, 14 ± 2%.

Subjects slept 32 ± 6% in the supine position and the rest of the time in the lateral position (no prone sleep was observed). The apnea-hypopnea index was below 5 in all 10 subjects.

As expected, total minute ventilation for the 10 subjects during wakefulness (5.9 ± 0.3 l/min) was higher than that during sleep [5.2 ± 0.2 l/min; mean difference 0.7 ± 0.1%, 95% confidence interval (CI) 0.5–0.9%, $P < 0.0001$]. However, there was no significant difference in minute ventilation between the different sleep stages (stage 2 sleep 5.3 ± 0.3, slow-wave sleep 5.2 ± 0.2, and REM sleep 5.2 ± 0.2 l/min) for the 10 subjects in this study (ANOVA $P = 0.63$) (Fig. 2). The change in minute ventilation between wakefulness and sleep was statistically significant in both men (wake 6.6 ± 0.1, sleep 5.8 ± 0.1 l/min; $P = 0.005$) and women (wake 5.2 ± 0.2, sleep 4.6 ± 0.1 l/min; $P = 0.005$). Minute ventilation for the men was significantly higher than that for the women during both wakefulness ($P = 0.006$) and sleep ($P = 0.007$).

Breathing pattern during sleep. There was no significant interaction ($P = 0.95$) between respiratory rate (breaths/min), sleep stage, and posture (supine or lateral position); the respiratory rate during wakefulness was 12.2 ± 0.7 and during sleep was 12.3 ± 0.5 in stage 2, 12.4 ± 0.5 in slow-wave sleep, and 13.8 ± 0.5 in REM sleep. Similarly, there was no significant interaction ($P = 0.35$) between tidal volume, sleep stage, and posture; the mean tidal volume during wakefulness was 0.50 ± 0.03 liters and during sleep was 0.43 ± 0.03 liters in stage 2, 0.43 ± 0.02 liters in slow-wave sleep and 0.39 ± 0.02 liters in REM sleep.

The grouped data for oral fraction of inhaled ventilation during wakefulness, stage 2, slow-wave sleep, and REM are illustrated in Fig. 3. Subjects inhaled primarily via the nasal route during both wakefulness and sleep, and the oral fraction during wakefulness (7.6 ± 4%) was not significantly different than that

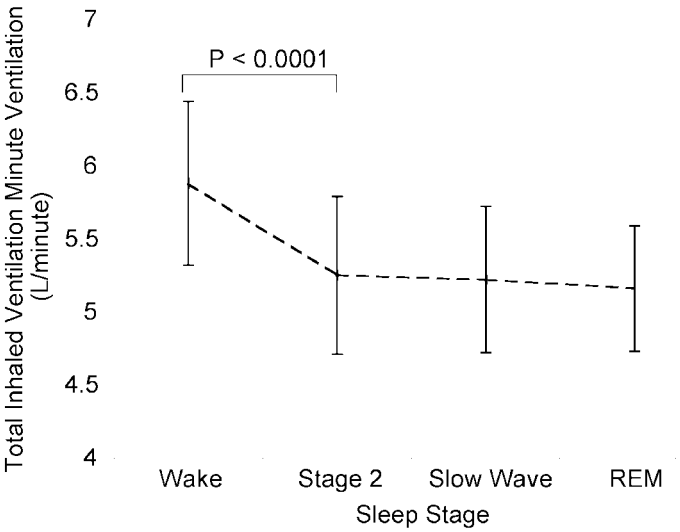

Fig. 2. Inhaled ventilation [means ± 95% confidence interval (CI)] during wakefulness and sleep in 10 normal subjects. Stage 2, stage 2 sleep; Slow Wave, stages 3 and 4 sleep; REM, rapid-eye-movement sleep.

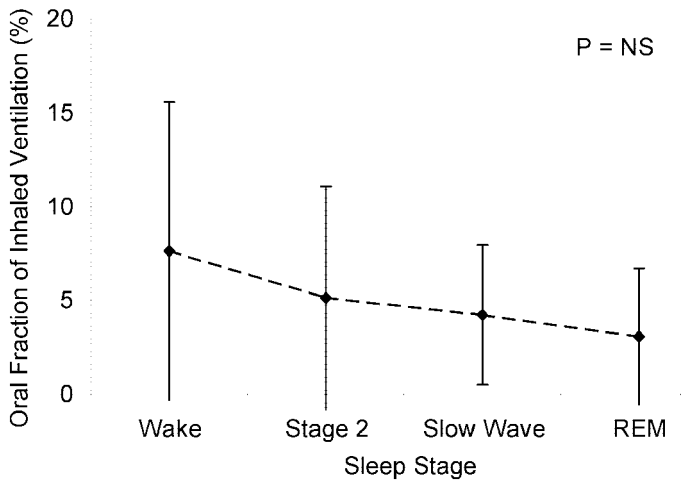

Fig. 3. Oral fraction of inhaled ventilation (mean ± 95% CI) during wakefulness and sleep in the 10 subjects.

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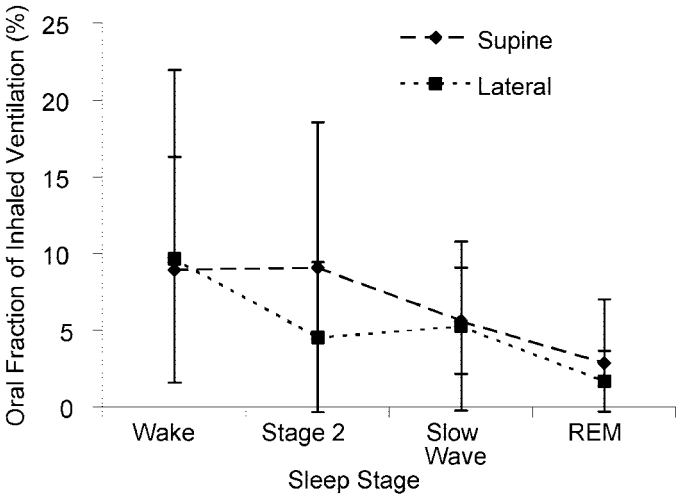

Fig. 4. Oral fraction of inhaled ventilation (mean ± 95% CI) during wakefulness and sleep in the supine and lateral positions. (Higher mean values compared with Fig. 3 result from use of data from different subjects while supine and lateral because several subjects did not have wake and all sleep stages in both supine and lateral positions).

during sleep (4.3 ± 2%; mean difference 3.3 ± 2%, 95% CI −2.1–8.8%, $P = 0.19$). No significant difference ($P = 0.14$) in the oral fraction was observed between different sleep stages: stage 2 5.1 ± 2.8%, 95% CI −5.9–11.1%; slow-wave 4.2 ± 1.8%, 95% CI 0.5–7.9%, REM 3.1 ± 1.7%, 95% CI −0.6–6.7%. No significant interaction ($P = 0.89$) was observed between the oral fraction, sleep stage, supine vs. lateral posture (Fig. 4), or gender ($P = 0.52$). The oral fraction during sleep in the five men was 2.7 ± 1.2%, and in the five women it was 5.8 ± 2.7%; mean difference 3.1 ± 2%; 95% CI −4.3–10.4%, $P = 0.32$.

The change in the oral fraction of inhaled ventilation between wakefulness and sleep was not significantly different in either the women (wake 11.8 ± 2%; sleep 5.8 ± 3%; mean difference 6.0%, 95% CI −6.9–19%, $P = 0.27$) or the men (wake 3.5 ± 2%, sleep 2.7 ± 1%; mean difference 0.8%, 95% CI −2.1–3.6%, $P = 0.49$).

The nasal resistance in the five male subjects (men 2.0 $cmH_2O \cdot l^{-1} \cdot s$) was similar to that of the five women (2.0 $cmH_2O \cdot l^{-1} \cdot s$; $P = 0.97$). In this small group of subjects, the nasal resistance did not correlate significantly with oral fraction during wakefulness or sleep.

Table 3 describes the statistical power of the present study to discriminate differences in oral fraction between sleep stages, sleeping position, and gender.

DISCUSSION

This paper is the first to describe partitioning of inhaled ventilation during sleep in a group of healthy subjects with documented normal nasal resistance at the time of the overnight sleep studies. The major finding is a striking predominance of nasal over oral inhaled ventilation during sleep, which did not change with sleep stage. There were no significant gender-related or posture-related differences in the inhaled oral fraction. Thus healthy subjects without sleep apnea and with normal nasal resistance demonstrate a marked predilection for the nasal breathing route over the oral one.

Only two other studies have measured oral ventilation (9) or mouth opening (12) during sleep in normal subjects. Gleeson and colleagues (9) measured simultaneous oral and nasal exhaled ventilation during sleep in seven men and seven women. Consistent with the findings in the present study, they reported that the oral fraction of exhaled ventilation did not change significantly between different sleep stages. In the latter study, men had a higher oral fraction than women during wakefulness and sleep, but when nasal resistance was measured in 8 of the 14 subjects, albeit distant from the time of the overnight recordings of oral and nasal ventilation, it was significantly higher in the five men than in the three female subjects. The latter finding may account for the higher oral fraction observed in the male subjects in that study (9) compared with the present study. The fact that several subjects in the latter study were regular snorers and one had polysomnographic obstructive sleep apnea may also account for the differences in oral fraction between that study and the present one. In particular, nasal resistance in the present study was not different between genders nor was the oral fraction during sleep.

Hollowell and Suratt (12) measured jaw opening during wakefulness and sleep in normal subjects and

Table 3. *Post hoc statistical power calculation*

Change in Oral Fraction with	Estimated Minimal Significant Difference, %	Standard Deviation for Observed Differences	Standardized Difference	Statistical Power, % ($\alpha = 0.05$)
State (sleep vs. wake)	10	7.56	1.32	84
Sleep stage (stage 2 vs. REM)	5	3.5	1.43	88
Body position (supine vs. lateral)	5	3.02	1.66	96
Gender				
Pooled over all stages	5	1.82	2.75	>99.5
Gender and sleep stage				
Wake	10	7.85	1.27	83
Stage 2	5	0.31	16.13	>99.5
Slow wave	5	1.01	4.95	>99.5
REM	5	1.70	2.94	>99.5
Sleep (pooled)	5	1.26	3.96	>99.5

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in patients with OSA, using a calibrated strain gauge placed vertically across the mouth. Jaw opening was observed to be greater at end inspiration than end expiration in normal subjects, but the mean difference was <0.5 mm (a distance that could potentially be accommodated by the elasticity of the facial skin and soft tissues, without necessitating opening of the lips). In the present study, there were many prolonged periods during sleep in which no appreciable mouth breathing occurred whatsoever. It is important to emphasize that mouth opening and mouth breathing are quite distinct entities. During quiet breathing, normal subjects and even subjects with increased nasal resistance may exhibit unequivocal mouth opening and simultaneous exclusive nasal breathing (18, 31). Hence the previous observation of jaw opening during sleep (12) is fully compatible with the observation of markedly predominant nasal inspiration throughout sleep in the present study.

The rationale for predominant nasal inhaled ventilation during sleep can be explained on the basis of anatomic and physiological changes during sleep. Movements of the soft palate are pivotal in determining oral and nasal airflow while awake and are under voluntary control (31); the more variable oral fraction during wakefulness than sleep in the present study is not, therefore, surprising. During sleep (both non-REM and REM), the EMG activity of the palatoglossus, levator palatini, and tensor palatini muscles (which alter the position of the soft palate) has been shown to decrease significantly (34, 35). Imaging studies of normal subjects reveal posterior displacement of the hypotonic soft palate during sleep such that the retropalatal site becomes the narrowest part of the upper airway (decreasing in volume by 19% on average, compared with wakefulness), whereas the dimensions of the retroglossal airway remain relatively unchanged (36). Hence the predominant nasal ventilation demonstrated in the present study occurs despite increased narrowing of the retropalatal airway during sleep. However, imaging of the upper airway during sleep in normal subjects has also revealed thickening of the lateral pharyngeal walls and tongue during sleep (36), which could potentially narrow or obstruct the oropharyngeal airway. Fluoroscopic imaging has demonstrated that, even while awake, there is apposition between the soft palate and tongue base in the recumbent position (31). Hence the marked predominance of nasal inhaled ventilation during sleep in the present study could be explained on an anatomic basis by narrowing or obstruction of the oropharyngeal airway during sleep in normal subjects, perhaps at the interface between the base of the tongue, lateral pharyngeal walls, and soft palate.

Physiological considerations may also help explain the observed predominance of nasal ventilation during sleep in normal subjects. First, it is important to understand that any reduction in upper airway resistance during oral breathing compared with nasal breathing relates only to wakefulness while oral breathing is conducted through a mouthpiece. There is no difference in upper airway resistance with breathing route when awake and breathing through a face mask, in either the erect or recumbent positions (1, 2). We are not aware of any reported comparisons of upper airway resistance during sleep with breathing route. However, mouth opening has been shown to increase the tendency to upper airway collapse (24) and to be associated with pharyngeal airway narrowing (15). The nasal route for inhalation may provide important afferent input to protect the upper airway from collapse because nasopharyngeal (and superior laryngeal nerve) afferents, but not oropharyngeal sources, contribute to the normal reflex augmentation of upper airway dilator muscle activity on exposure to a negative pressure stimulus (the "negative pressure reflex") (13, 16, 22). There is considerable evidence that such local reflex mechanisms are important in upper airway integrity: *1*) there is a marked reduction in upper airway dilator muscle activation during breathing via tracheostomy compared with normal (20, 21); *2*) the increased genioglossal activity in response to application of negative pressure to the upper airway (37) can be abolished with topical mucosal anesthesia (8); and *3*) application of topical mucosal anesthesia to the nasal airway results in a significantly increased propensity to upper airway collapse during sleep in otherwise healthy normal subjects (38). Basner and colleagues (3) reported an increase in alae nasae and genioglossal activation during nasal breathing in awake normal subjects, compared with oral breathing, which was abolished with topical lidocaine applied to the nasal mucosa, suggesting reflex activation of the genioglossus via nasal mucosal receptors. However, more recent studies that confirmed the physiological increase in alae nasae activation with increased nasal airflow did not corroborate the finding of increased genioglossal activation with the nasal breathing route (32, 40).

Despite the latter somewhat ambiguous physiological findings, clinical studies and studies of normal subjects have consistently demonstrated a greater predisposition to upper airway obstruction during sleep while mouth breathing (5, 17, 23, 29, 33, 39, 41). Most of these studies employed artificial obstruction of the nose (with inflated balloons; Ref. 41), gauze soaked in petroleum jelly (5, 29, 33, 39), or tape around the nares (17), but similar findings were reported during naturally occurring nasal obstruction in patients with seasonal allergic rhinitis (23).

Hence, although the mechanisms underlying the observation in normal subjects of predominant nasal inhalation during sleep in the present paper have not been not fully elucidated, there are several plausible advantages, both anatomic and physiological, of predominant nasal ventilation. In addition, the disadvantage of oral breathing to the integrity of the upper airway during sleep in normal subjects has been consistently documented.

This study can be criticized on several grounds. Subjects do not normally sleep with a face mask, and the dead space and cutaneous stimulation associated with the face mask could alter ventilation during sleep. The

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face mask employed during the present study was contoured to the face and nose in an attempt to minimize dead space, and it had a lower dead space than similar oronasal masks previously employed to measure ventilation during sleep (9, 38). The resulting minute ventilation measurements in this study are much closer to normal resting minute ventilation measurements than those previously reported (9). Unfortunately, from a practical perspective, there is no way of simultaneously measuring oral and nasal ventilation during sleep without employing a compartmentalized face mask.

A second potential criticism of the present study is that the low reported oral fraction of inhaled ventilation could imply that the face mask restricted mouth opening. We feel certain that this is not the case for two reasons: *1*) every subject was observed to open the mouth widely on request with the mask sealed in place, before the pneumotach was replaced in the oral port of the mask to begin the study (subjects were specifically asked whether they perceived any restriction to normal breathing through either the nasal or oral airways with the face mask in place before the start of the study, and the study did not commence until the face mask was adjusted and sealed in a position with which the subject perceived oral and nasal breathing to be completely unrestricted). *2*) When the results demonstrating a low oral fraction in normal subjects became evident, to ensure that mouth opening was not restricted during sleep with the present mask system, we studied another healthy subject without clinical or polysomnographic evidence of OSA but with higher than normal nasal resistance (4.6 $cmH_2O \cdot l^{-1} \cdot s$ while seated, awake). Figure 5 demonstrates this subject's oral fraction of inhaled ventilation during wakefulness and sleep. Thus mouth breathing was clearly feasible during sleep with the experimental setup used in these 10 normal subjects during sleep, and the low reported oral fraction appears to be bona fide and not an artifact caused by restriction of mouth opening during sleep by the face mask. A third potential criticism of the present study is that nasal resistance was not measured in the recumbent position, the position in which subjects sleep. The main reason for measuring nasal resistance in this study was simply to document that it fell within normal limits, so that we could then define oral and nasal partitioning of inhaled ventilation in truly normal subjects. The seated position is normally used for nasal resistance measurement in clinical practice and provides the reference point for comparison with normative data, hence the reason for measuring it in that position. Nonetheless, the recumbent nasal resistance would be more relevant to sleep, and some of the variability in the oral fraction between wakefulness and sleep (a nonsignificant decrement in oral fraction among both genders) may have resulted from simultaneous changes in nasal resistance. Without measurement of nasal resistance and oral fraction, during wakefulness and sleep, this question cannot be answered. It is worthy of note, however, that previous work has demonstrated no significant change in nasal resistance between wakefulness and sleep, or between different sleep stages, in normal subjects or snorers (14, 25). In addition, whereas nasal resistance tends to increase in the recumbent position compared with the erect position, the postural change in nasal resistance among normal nonatopic subjects is very small (6).

Finally, as Table 3 illustrates, the study was adequately powered to detect only moderately large differences ($\geq$10%) in oral fraction between wakefulness and sleep (because of the marked variability in oral fraction while under voluntary control during wakefulness). However, it was adequately powered to detect small changes (5%) in oral fraction between sleep stages, and this was the primary objective of the study.

In summary, this study describes partitioning of inhaled ventilation between the nose and mouth during sleep in healthy subjects with normal nasal resis-

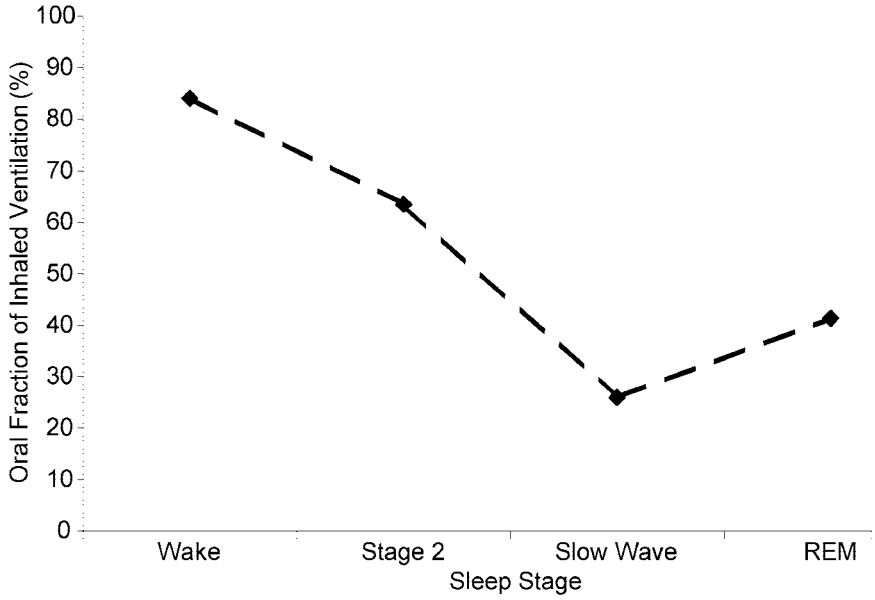

Fig. 5. Oral fraction of inhaled ventilation during wakefulness and sleep in a male subject with nasal resistance of 4.6 $cmH_2O \cdot l^{-1} \cdot s$.

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tance. The study demonstrates a marked preponderance for nasal inhalation over oral inhalation during sleep, which does not change significantly with sleep stage or position.

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