Impact of age on breathing and resistive pressure in people with and without sleep apnea

HELEN A. K. BROWNE, LEWIS ADAMS, ANITA K. SIMONDS, and MARY J. MORRELL. Impact of age on breathing and resistive pressure in people with and without sleep apnea. J Appl Physiol 90: 1074–1082, 2001.—We investigated the effect of age on breathing and total pulmonary resistance (R_l) during sleep by studying elderly (≥65 yr) and young (25–38 yr) people without sleep apnea (EN and YN, respectively) matched for body mass index (BMI). To determine the impact of sleep apnea on age-related changes in breathing, we studied elderly and young apneic patients (EA and YA, respectively) matched for apnea and BMI. In all groups (n = 11), breathing during periods of stable sleep was analyzed to evaluate the intrinsic variability of respiratory control mechanisms. In the absence of sleep apnea, the variability of the breathing was similar in the elderly and young [mean (± SD) coefficient of variation (CV) of tidal volume (VT); wake: EN 21.0 ± 14.9%, YN 14.7 ± 5.5%; sleep: EN 14.0 ± 6.0%, YN 11.5 ± 6.4%]. In patients with sleep apnea, breathing during stable sleep was more irregular, but there were no age-related differences (CV of VT; wake: EA 22.0 ± 11.6%, YA 16.7 ± 11.3%; sleep: EA 32.8 ± 24.9%, YA 25.2 ± 16.3%). In addition, EN tended to have a higher R_l (n = 6, R_l midinspiration, wake: EN 7.1 ± 3.0, YN 9.1 ± 6.4 cmH2O·L−1·s−1, sleep: EN 17.5 ± 11.7, YN 9.8 ± 2.0 cmH2O·L−1·s−1). We conclude that aging per se does not contribute to the intrinsic variability of respiratory control mechanisms, although there may be a lower probability of finding elderly people without respiratory instability.

The estimated prevalence of sleep-disordered breathing, defined as an apnea-hypopnea index (AHI) >10 events/h, in a working population of young people between the ages of 30 and 39 yr is 5% of women and 12% of men (39). In the elderly, the prevalence of sleep-disordered breathing ranges between 13 and 39% (1, 4, 9, 10, 12, 16, 31). The wide variation in these estimates is likely to reflect the different health status of the elderly populations studied, the methods used to measure breathing, and the definitions of the disease. Using similar study methods and disease criteria, Bixler et al. (4) estimated the prevalence of sleep apnea (AHI >10 events/h) to be 24% in elderly men (65–100 yr) compared with 3% in a younger population (20–44 yr).

Despite this age-related increase, little is known about the etiology of sleep-disordered breathing in the elderly. In middle-aged people, the majority of sleep apnea is due to obstruction of the upper airway, whereas in the elderly, the occurrence of central apneas is greater (4), but the sleep apnea remains predominantly obstructive (15, 16). This suggests that the higher prevalence of sleep apnea in the elderly may result from an increased propensity of the upper airway to collapse during sleep. The finding that pharyngeal resistance increases with age is consistent with this idea (34, 36). On the other hand, sleep in the elderly is more fragmented because of a decrease in the arousal threshold and an increase in the amount of light sleep (6). Changes in sleep patterns have been shown to be associated with respiratory periodicity (28), suggesting that fluctuations in sleep state could modulate central respiratory drive (i.e., leading to central apneas). A further possibility is that aging may be associated with a greater instability of central respiratory control mechanisms, perhaps secondary to changes in ventilatory chemosensitivity or circulatory changes. Support for this mechanism is provided by the observation that breathing is more irregular in elderly compared with younger people (14, 33).

The aim of the present study was to investigate the effect of age on the respiratory pattern and upper airway resistance during sleep under carefully controlled conditions. To achieve this, we studied elderly and young people without sleep apnea, matched for body mass index (BMI). Additionally, to determine the impact of sleep apnea on age-related changes in breathing during sleep, we also studied groups of elderly and young patients matched for the severity of sleep apnea and BMI. In all groups, we focused on breathing during periods of stable sleep to evaluate the intrinsic variability in breathing pattern and upper airway resistance. We hypothesized that, in the absence of sleep apnea, breathing would be more irregular in the elderly and that this would be associated with greater fluctuations in airway resistance. We further hypothesized that the presence of sleep apnea would potentiate any age-related breathing instability.
METHODS

Subjects. Four groups (n = 11) were studied on two separate occasions. A group of elderly (>65 yr) and a group of young (25–38 yr) patients with sleep apnea (EA and YA, respectively) were recruited from local sleep clinics. For each of the elderly and young patient groups, age-matched normal volunteers without sleep apnea (EN and YN, respectively) were studied; these individuals were recruited from the general population via advertisements placed around the hospital and in the local paper. Sleep apnea was defined as an AHI >10 events/h of sleep. The absence of apnea was defined as an AHI <6 events/h. Any volunteer recruited to one of the normal groups who was subsequently found to have an AHI >10 events/h was moved to the relevant apneic group. The EA and YA groups were matched for AHI; all four groups were matched for BMI. All subjects had had no neurological disease or any complaints of chronic pain that could have influenced their sleep quality. Four EA patients, two EN volunteers, and one YA patient had hypertension, which was treated with medication.

Measurements. All subjects were studied twice. The first study was a standard overnight polysomnogram to determine the presence or absence of sleep apnea. Measurements of sleep and breathing were made using a computerized sleep acquisition system (Sleeplab 1000p, Erich Jaeger, Markt Harborough, UK). Sleep was monitored using two electroencephalograms (EEG; C3-A2, C4-A1), two electrooculograms (EOG; left and right eye), and an electromyogram (EMG) of the submental muscle. Chest wall and abdominal movements were monitored using pneumotachobands. An index of respiratory muscle effort was obtained from an EMG positioned on the surface of the chest, either in the midclavicular or midaxillary line in the sixth to eighth intercostal space. An index of expired airflow from the nose and mouth was recorded using a thermistor placed above the top lip. Tracheal sounds were recorded using a microphone taped in position on the neck to the side of the trachea. Arterial oxygen saturation was estimated using a finger pulse oximeter (model Biox 3700e, Ohmeda). Leg movements were recorded using an EMG positioned over the left tibial muscle. All signals were stored digitally using commercial Jaeger software.

A second sleep study was performed to make quantitative measurements of sleep-related changes in breathing and resistance to airflow. Sleep state was recorded using the electrode placements described for the first study (see above) via analog amplifiers (model 12e-8-23, Grass Instrument, Warwick, MA). Airflow was measured using a Fleisch no. 2 pneumotachometer with a differential pressure transducer (MP45, ±2 cmH2O, Validyne) attached to a nasal mask. Expired air was sampled through a flexible probe placed just within the nostril. From this, end-tidal Pco2 (PetCO2) was measured using a rapid-response infrared gas analyzer (Capnograph, P. K. Morgan); this was taken as an estimate of Pco2 in arterial blood. The dead space of the mask plus pneumotachograph was ~60 ml.

Esophageal pressure (Pes), reflecting intrathoracic pressure, was measured via a catheter with a pressure transducer at the tip (CTC/6F; Gaeltec, Isle of Skye, Scotland). This measurement was used to calculate total pulmonary resistance (Rt) based on the methods described by Neergaard and Wirz (26). Before passing the catheter, we sprayed both nasal passages and the back of the throat with a small amount of topical anesthetic (4% lidocaine hydrochloride solution, Astra Pharmaceuticals, Hertfordshire, UK). The catheter was then passed through the nasal passage until the tip of the catheter was 40 cm from the nostril. The digitized Pes and airflow signals were analyzed off-line to produce a continuous measure of Rt. \((Pes - V/C)/V\), where V is the instantaneous volume of the breath integrated from airflow, C is the dynamic compliance of the breath, and V is instantaneous airflow. This computerized method of deriving Rt. was based on the techniques of Mead and Whittenberger (21). For the purposes of this study, we considered Rt to be the lung tissue resistance plus the airway resistance, including upper airway resistance. The mean inspiratory Rt. was calculated by dividing inspiration (defined using flow crossing zero) into nine equal points; the middle seven values were then averaged \((R_{t,midisp})\). The Rt. at the peak of the negative inspiratory pressure \((R_{t,peakisp})\) was also calculated. It is likely that for some breaths, especially in the apneic volunteers during sleep, the relationship between Pes and airflow may not have been linear for our measurements of Rt. Nevertheless, previous studies have shown that Rt. calculated in this way will reflect that total “load” on the respiratory system (23).

All signals were recorded on a digital computer via an analog-to-digital interface (model 1401 Plus, Cambridge Electronic Design, Cambridge, UK). Digital signals were then analyzed (see Analysis) using commercially written software (Spire 2, Cambridge Electronic Design).

Protocol. All subjects were interviewed, and estimates of lung function were made before the first overnight study. They were also asked to refrain from drinking alcohol or coffee 4 h before the study. After application of transducers, standard overnight polysomnography was carried out; sleeping position was not restricted. The results of this sleep study were used to determine the presence or absence of sleep apnea.

The second overnight sleep study was carried out within an average of 48 ± 9 (SD) days of the first study. Before this study, subjects were asked to restrict their sleep (maximum 4 h) on the previous night. They were also asked to eat only a light meal 4 h before attending the laboratory and reminded to avoid coffee and alcohol. Subjects arrived at the sleep laboratory 1–2 h before their normal sleep time. After the application of the EEG, EOG, and EMG electrodes, and the passing of the esophageal catheter, subjects lay supine on the bed. Nasal drops (Otrivine, Novartis Consumer Health, Macclesfield, UK) were applied to reduce secretions, the PETCO2 probe was then secured, and a nasal mask and headgear were fitted. To check that the mask was airtight, the subject was asked to attempt to breathe when the opening of the mask was occluded. When any leaks had been eliminated, the pneumotachometer was attached to the nasal mask. The subject was then allowed to fall asleep. All subjects slept in the supine position during the second study.

Analysis. The first sleep study was analyzed to determine the AHI for each subject. The sleep stage was determined from computer recordings of the EEG, EOG, and EMG, according to standard criteria (30). An apnea was defined as a cessation of airflow for >10 s. A hypopnea was defined as a >50% reduction in airflow for >10 s. The number of apneas and hypopneas were divided by the total sleep time to calculate the AHI. The apneas were further classified as obstructive or central, based on the presence or absence of respiratory effort during the apnea; chest wall and abdominal movements, surface respiratory muscle EMG, and snoring were used as markers of respiratory effort.

Data from the second sleep study were analyzed to quantify breathing during stable sleep. The sleep stage was scored according to standard criteria (30). Breath-by-breath mea-
measurements of breathing variables (total breath time ($T_{tot}$), tidal volume ($V_t$), inspired minute ventilation ($V_i$), $\text{PET}_{CO_2}$, plus $R_{midinsp}$ and $R_{peakinsp}$) were made from periods of wakefulness and non-rapid-eye-movement (NREM) stage 2 sleep that were >1 but <5 min in duration. Sleep periods were sampled only if sleep had been established >2 min and contained no brief cortical arousals as defined by standard criteria (35). Between two and five sleep periods were analyzed for each subject. The periods of sleep chosen for analysis were selected by a researcher blinded to the breathing pattern and subject group. Each study was first staged for sleep and arousals, and the sleep periods that met the above criteria were marked. The EEG was then checked for arousals by a second researcher, and the breathing was analyzed. Where more than five sleep periods met the analysis criteria, the data were selected across the night from different periods of stable sleep. All wakefulness periods throughout the night were also scored by a researcher blinded to the breathing pattern and subject group. Any epochs of wakefulness containing periods of theta activity >3 s were excluded. The wakefulness periods were selected based on their proximity in time to the sleep periods. Where a sleep period was bounded at the beginning and end by wakefulness, the wakefulness period preceding sleep was selected for analysis. Between two and three wakefulness periods were analyzed for each subject; the number of periods available for analysis was limited because of the tendency of subjects to fall asleep during the wakefulness recordings. The variability in breathing during the analysis periods was assessed by calculating the coefficient of variation for all breaths within each period.

Statistical analysis. For each respiratory variable, the group mean data were compared using an ANOVA. The influence of sleep on breathing was examined with respect to “age” (elderly and young) and “disease status” (apnea and nonapnea) as two between factors and to “state” (wakefulness and NREM) as a within factor. A post hoc analysis was then conducted on the variables that showed a statistically significant influence of state with disease status. We performed separate ANOVAs for the apneic and nonapneic groups, with age as the between factor and state as a within factor. There were no significant interactions between state with age were seen in the initial ANOVA.) Statistical significance was defined as $P < 0.05$.

RESULTS

Subjects. A total of 56 subjects were recruited to take part in our study. Twelve subjects were excluded from the final analysis ($YA = 3$, $EN = 5$, $EA = 4$); this was due to sickness ($n = 1$), no suitable periods of stable sleep ($n = 7$), technical failure ($n = 2$), or unwillingness to continue the study ($n = 2$). The sleep characteristics from the 44 representative subjects are shown in Table 1. All four groups were matched for BMI; however, the neck circumference of the YN group was significantly smaller compared with the YA group (paired $t$-test, $P = 0.03$).

Sleep-related changes in breathing. The group mean (± SD) sleep-related changes in breathing are shown in Fig. 1. Consistent with our previous study, we found that in all groups combined sleep was associated with a significant shortening of $T_{tot}$ ($P = 0.04$) and a reduction in $V_t$ ($P = 0.001$); this produced an overall reduction in $V_i$ ($P = 0.001$) and an increase in $\text{PET}_{CO_2}$ ($P = 0.001$; $n = 9$) (23). However, the magnitude of the sleep-related changes was not significantly different in the elderly compared with the young groups or in the apneic compared with the nonapneic groups.

For each group, the influence of sleep on the coefficient of variation of each variable measured is shown in Fig. 2. In the apneic groups ($EA$ and $YA$ combined), breathing during stable sleep was significantly more variable ($T_{tot}$, $P = 0.01$; $V_t$, $P = 0.03$; $V_i$, $P = 0.01$). Whereas in the nonapneic groups ($EN$ and $YN$ combined), sleep was associated with a reduction in variability ($T_{tot}$, $P = 0.001$; $V_t$, $P = 0.03$). There was no significant difference in the variability of breathing in the elderly vs. young groups.

Sleep-related changes in $R_{midinsp}$ and $R_{peakinsp}$ In 16 of the 44 subjects (36%), we were unable to calculate $R_i$; this was a result of the technically poor quality of the Pes measurements during sleep. Because the breathing analysis compared equal-sized groups matched for age and BMI, we took care to ensure that these variables were also matched for the analysis of $R_i$ data. This resulted in $n = 6$ for each group with the following characteristics: age, $EN$ 70 ± 4.9, $EA$ 68 ± 2.6, $YN$ 31 ± 1.9, and $YA$ 32 ± 4.0 yr; BMI, $EN$ 27.7 ± 3.7, $EA$ 26.7 ± 2.3, $YN$ 26.1 ± 2.4, and $YA$ 31.6 ± 6.9 kg/m². The four subjects excluded from the analysis were $EN = 2$, $YN = 1$, and $YA = 1$ (age, $EN$ 65 and 67, $YN$ 31, and $YA$ 36 yr; BMI, $EN$ 24.5, 30.8, $YN$ 25.0, and $YA$ 27.7 kg/m²).

For each group, the mean $R_{midinsp}$ and $R_{peakinsp}$ obtained during wakefulness and sleep, are shown in the Table 1. Clinical and anthropometric data for elderly and young subjects with and without sleep apnea

<table>
<thead>
<tr>
<th>Group</th>
<th>Age, yr</th>
<th>Female/Male</th>
<th>BMI, kg/m²</th>
<th>Neck Size, cm</th>
<th>Significant Medical History</th>
<th>Blood Pressure, mmHg</th>
<th>Total Sleep Time (1st Study), h</th>
<th>AHI, events/h</th>
<th>Central Apnea, %</th>
<th>Obstructive Apnea, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA</td>
<td>70 ± 3.8</td>
<td>2/9</td>
<td>28.4 ± 2.0</td>
<td>41.2 ± 3.1</td>
<td>4 = Hypertension</td>
<td>123 ± 7.2</td>
<td>62 ± 0.6</td>
<td>26.3 ± 9.1</td>
<td>8.4 ± 9.8</td>
<td>28.2 ± 16.0</td>
</tr>
<tr>
<td>EN</td>
<td>69 ± 4.0</td>
<td>0/11</td>
<td>27.0 ± 4.0</td>
<td>41.2 ± 2.5</td>
<td>2 = Hypertension</td>
<td>133 ± 6.8</td>
<td>5.5 ± 1.2</td>
<td>2.6 ± 2.1</td>
<td>27.5 ± 32.0</td>
<td>19.2 ± 21.4</td>
</tr>
<tr>
<td>YA</td>
<td>32 ± 3.7</td>
<td>1/10</td>
<td>28.9 ± 5.9</td>
<td>40.6 ± 4.1</td>
<td>1 = Hypertension</td>
<td>117 ± 10.3</td>
<td>6.3 ± 1.3</td>
<td>25.0 ± 20.3</td>
<td>3.1 ± 5.2</td>
<td>9.1 ± 17.6</td>
</tr>
<tr>
<td>YN</td>
<td>32 ± 2.3</td>
<td>4/7</td>
<td>26.1 ± 2.9</td>
<td>36.4 ± 2.6</td>
<td>Nil</td>
<td>120 ± 7.8</td>
<td>6.0 ± 1.1</td>
<td>1.9 ± 2.0</td>
<td>37.7 ± 38.5</td>
<td>9.4 ± 30.1</td>
</tr>
</tbody>
</table>

Values are means ± SD. EA, elderly sleep apneic patients; EN, elderly people without sleep apnea; YA, young sleep apneic patients; YN, young people without sleep apnea; BMI, body mass index; AHI, apnea-hypopnea index.
Fig. 3A. Sleep was associated with an increase in both $R_I^{\text{midinsp}}$ and $R_I^{\text{peakinsp}}$, which was larger in the apneic groups ($R_I^{\text{midinsp}} P = 0.001; R_I^{\text{peakinsp}} P = 0.001$) compared with the nonapneic groups ($R_I^{\text{midinsp}} P = 0.05; R_I^{\text{peakinsp}} P = 0.01$). In the normal subjects, the magnitude of the increase was greater in the elderly compared with the young group (EN vs. YN), although this difference just failed to reach statistical significance, possibly because of the small sample size ($R_I^{\text{midinsp}} P = 0.07; R_I^{\text{peakinsp}} P = 0.09$). Examples of breathing in an EN person and a YN person are shown in Fig. 4. In the EN subject, during sleep, $P_{es}$ becomes more negative whereas $V$ remains constant (A); inspection of the relationship between Pes and $V$ shows that flow limitation is occurring (B), resulting in an increase in $R_I$ (C). This does not occur in the younger person, despite the fact that the two subjects are matched for BMI and AHI.

For each group, the coefficients of variation of $R_I^{\text{midinsp}}$ and $R_I^{\text{peakinsp}}$ obtained during wakefulness and sleep are shown in Fig. 3B. In the apneic group (EA and YA combined), breathing during stable sleep was significantly more variable ($R_I^{\text{midinsp}} P = 0.006; R_I^{\text{peakinsp}} P = 0.003$), this was not the case in the nonapneic group (EN and YN combined; $R_I^{\text{midinsp}} P = 0.96; R_I^{\text{peakinsp}} P = 0.87$). There was no significant difference in the variability of $R_I^{\text{midinsp}}$ and $R_I^{\text{peakinsp}}$ in the elderly vs. young groups.

**DISCUSSION**

In the present study, we set out to investigate the influence of age on breathing and airway resistance during sleep and how the presence of sleep apnea syndrome might impact on this. Overall, we found that during stable sleep elderly people did not breathe differently from younger people with the same BMI and that this applied to both the apneic and nonapneic groups. However, both elderly and young apneic groups did breathe more irregularly than their healthy counterparts during stable sleep. In addition, we found that nonapneic elderly people tended to have a larger sleep-related increase in $R_I$ compared with a younger group. This age-related effect was not seen in the apneic groups.

To interpret the results of the present study, it is necessary to consider the design of the experiment. We carefully selected the subjects taking part in our study to ensure that they conformed to our inclusion and exclusion criteria. By doing this, we were able to sep-
arate the impact of aging per se on breathing during sleep vs. the effect of sleep-disordered breathing. However, this approach does not allow us to measure the prevalence of sleep-disordered breathing in elderly people.

Respiratory instability during stable sleep. We wished to study intrinsic respiratory control during stable sleep. Critical to this approach was the need to ensure that periods of wakefulness and sleep did not contain any fluctuations in state. During sleep, we used the American Sleep Disorders Association criteria to define arousals (35). There is a lack of agreement in what constitutes a cortical arousal (18), and in so-called autonomic arousals no change in EEG frequency is visible (20). We chose the American Sleep Disorders Association criteria because these were arrived at by consensus agreement, and the inter scorer reliability is higher than that which occurs with shorter arousals (18). On the other hand, these criteria do not allow us to rule out the possibility that autonomic arousals occurred during our analysis periods. During wakefulness, we also chose a >3-s criterion for the appearance of theta activity in the waking EEG. We did this to be consistent with our sleep criteria. There are few reports of wakefulness criteria in the literature, and it is interesting that this strategy severely limited the amount of wakefulness data available for analysis across all groups.

In our study, aging was not associated with an increase in the intrinsic variability of breathing or Rl. These findings are consistent with those reported by Shore et al. (33); however, at first sight they appear to contradict the observations of Hudgel et al. (14). These workers reported a sleep-related increase in the variability of ventilation and upper airway resistance in elderly subjects. The difference between the findings of Hudgel et al. and those in our study may have been due to the selection of subjects. In our study, subjects were classified according to AHI; the elderly and young normal groups (i.e., those without apnea) had a mean AHI <2 events/h. In the study by Hudgel et al., the elderly subjects had a relatively high number of respiratory events (mean AHI >9 events/h) compared with the younger subjects (mean AHI <1 event/h); this difference is likely to have been reflected in the sleep-related variability of breathing. We also saw a sleep-related increase in the intrinsic variability of breathing in our elderly patients with sleep apnea.

The variability of breathing that occurs during stable sleep in both the elderly and young sleep apneic
patients may reflect an intrinsic instability of respiratory control mechanisms that is independent of any increase in upper airway resistance. Support for this idea comes from the recent observation that central apnea and periodic breathing can be produced in patients with severe sleep apnea by using a combination of proportional-assist ventilation to perturb breathing and continuous positive airway pressure to maintain the caliber of the upper airway (38). In normal people, using the same protocol, periodic breathing occurs infrequently (22). It is possible that the variability of breathing in their sleep apnea patients, which was unmasked by the use of proportional-assist ventilation, is associated with an augmentation of chemosensitivity. However, in apneic patients, the hypercapnic ventilatory response has been reported as increased (2), decreased (27), and no different (3), compared with normal people. In the elderly, during wakefulness the ventilatory response to hypercapnia and hypoxia is reduced, compared with younger people (7, 17, 25). On the face of it, this would tend to favor the stabilization of breathing, although it should be noted that the only study in which the ventilatory response to hypercapnia has been measured during sleep reported no difference between elderly and young people (25).

An alternative explanation for the variable breathing observed in the apneic patients is that they had a sleep-related reduction in the caliber of the upper airway that resulted in airflow limitation but that the associated decrement in VT was insufficient to be classified as a hypopnea. In fact, we did find that the variability of breathing in our apneic patients was associated with variability in RL. This suggests that the breathing was determined by the intrinsic instability of the upper airway; however, this instability was not age dependent. Evidence for the occurrence of airflow limitation in normal elderly people can be seen in the pressure-flow relationship in Fig. 4B.

Respiratory instability associated with arousal and sleep onset. In the present study, we focused on breathing during periods of stable sleep to evaluate the intrinsic variability in breathing pattern and upper airway resistance. In taking this approach, by definition we have not investigated the influence of sleep onset or of arousal on respiratory control. In elderly people, changes in VT coincide with fluctuations in EEG frequency (28), and arousals are more often associated with respiratory disturbance (24). These observations suggest that transitions between wakefulness and sleep may have a greater influence on respiratory con-
Fig. 4. A: original recordings for a YN (top) and an EN (bottom) subject during wakefulness and stable non-rapid-eye-movement sleep. EEG, electroencephalograph; \( V \), instantaneous airflow; Pes, esophageal pressure. Note, Pes is more negative during sleep in the EN compared with the YN subject. B: Pes (resistive pressure) and \( V \) (flow) plots for the individual breaths shown in A; plots from the EN subject show pronounced flow limitation during non-rapid-eye-movement sleep. C: plots (means ± SD) for \( R_{\text{pulmonary}} \) for all the breaths shown in A plotted over the inspiratory time. In the group analysis, the 8 values were averaged to produce a single value for total pulmonary resistance.
trol mechanisms in elderly compared with younger people. If this were the case, then it is the impact of age on sleep, that leads to the increased prevalence of sleep-disordered breathing in healthy elderly people without cardiovascular, neurological, or other respiratory diseases. However, it is unlikely that all individuals with disturbed sleep have sleep apnea syndrome; therefore, a critical interaction between the sleep-wake instability and respiratory control vulnerability must occur. In elderly people, the tendency toward airflow limitation and a higher $R_L$ may contribute to the respiratory control vulnerability.

Age-related changes in $R_L$. We have shown that elderly people without sleep apnea tend to have a higher $R_L$ during sleep compared with younger people. This finding is consistent with previous studies that have found that during sleep there is an age-related increase in upper airway resistance and an age-related decrease in the activity in the genioglossus tensor palatini muscles (34, 37). However, other studies during wakefulness (8, 36) and sleep (14) have reported that the upper airway resistance and genioglossus activity during quiet breathing are similar in elderly and young people. It has been suggested that any age-related increase in upper airway resistance may be compensated for by a greater activation of the genioglossus muscle in response to negative pressure (8). This may be the mechanism whereby some elderly people are able to compensate for an age-related respiratory control vulnerability.

The aging process is associated with a loss of strength in the skeletal muscles (13) and, to a lesser extent, in the diaphragm (29). It is possible that the strength of the upper airway dilator muscles is also reduced in the elderly; however, if this were the case, we would have expected to observe a higher upper airway resistance in the elderly normal group during wakefulness. The aging process is also associated with changes in respiratory mechanics; for example, chest wall compliance is likely to be reduced and residual volume is increased (11). These age-related changes in lung function would have influenced the $R_L$ in our elderly people to a greater or lesser extent. The fact that during wakefulness we saw no difference in $R_L$ between all the groups indicates that they were of minimal relevance.

Aging is associated with changes in the regulation of adipose tissue that results in an increase in body fat (5); to allow for this potentially confounding influence, we matched our groups for BMI. Despite this careful matching, we still found that neck circumference was larger in the young apneic patients compared with the young normal subjects; interestingly, the elderly groups had similar neck sizes, which were larger than those of the young healthy subjects. This observation is consistent with preliminary data showing that in elderly subjects fat is preferentially deposited in the upper airway compared with younger subjects (19). If this is the case, then even elderly subjects with a normal BMI may have a thick neck. Such a difference in fat distribution may account for our finding of an increased $R_L$ in elderly normal subjects compared with young normal subjects.

Possible implications of our findings. We have shown that aging per se does not contribute to instability of breathing during established stable sleep. This finding supports the idea that the high prevalence of sleep-disordered breathing in the elderly occurs because the incidence of disorders that are associated with sleep-disordered breathing, such as heart failure, is higher. On the other hand, it may be related to a critical interaction between the greater sleep-wake instability in the elderly and to a respiratory control vulnerability. The tendency of elderly people to have a larger wake-to-sleep difference in upper airway resistance might contribute to this; however, by limiting our study to stable sleep, we have not directly tested this latter suggestion. Some elderly people are clearly able to adapt to the interaction, as in our elderly normal group. However, those that do not will contribute to the high prevalence of sleep-disordered breathing in the otherwise healthy elderly.

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