Activity of respiratory pump and upper airway muscles during sleep onset

CHRISTOPHER WORSNOP, AMANDA KAY, ROBERT PIERCE, YOUNG KIM, AND JOHN TRINDER

Department of Respiratory Medicine, Austin and Repatriation Medical Centre, Heidelberg, Victoria 3084; and School of Behavioural Science, The University of Melbourne, Parkville, Victoria 3052, Australia

Worsnop, Christopher, Amanda Kay, Robert Pierce, Young Kim, and John Trinder. Activity of respiratory pump and upper airway muscles during sleep onset. J. Appl. Physiol. 85(3): 908–920, 1998.—Ventilation decreases at sleep onset. This change is initiated abruptly at α-θ electroencephalographic transitions. The aim of this study was to determine the contributions of reduced activity in respiratory pump muscles and upper airway dilator muscles to this change. Surface electromyograms over the diaphragm (Di) and intercostal muscles and fine-wire intramuscular electrodes in genioglossus (GG) and tensor palatini (TP) muscles were recorded in nine healthy young men. It was shown that phasic Di and both phasic and tonic TP activities were lower during θ than during α activity. Breath-by-breath analysis of the changes at α-θ transitions during the sleep-onset period showed a number of changes. At α-θ transitions, phasic activity of Di, intercostal, and GG muscles fell and rose again, and phasic and tonic activities of TP fell and remained at low levels during θ. With a state transition from θ to α, the phasic and tonic activities of the Di, GG, and TP increased dramatically. It is now clear that the fall in ventilation that occurs with sleep is related to a fall in activities of both upper airway dilator muscles and respiratory pump muscles.

VENTILATION (\(\dot{V}\)) is lower in stable sleep compared with wakefulness (10, 16). As arterial PCO₂ is higher in sleep than in wakefulness (21), the reduced \(\dot{V}\) cannot simply be due to reduced CO₂ production associated with the reduced metabolic activity during sleep (5). Upper airway resistance (UAR) is increased in stable sleep (16), and this rise is thought to be due to narrowing of the upper airway (UA) as a consequence of reduced tone in the UA dilator muscles, which allow the negative pressure generated by diaphragm (Di) activation to collapse the UA (10, 30). Inspiratory pump muscle activity is also higher in stable sleep than in wakefulness (8, 22, 26), but as \(\dot{V}\) is lower, compensation by the respiratory muscles for the increased UAR can be considered to be incomplete (7). Because of the increased inspiratory muscle activity in sleep, increased UAR, rather than reduced drive to inspiratory muscles, has been thought to explain the reduced \(\dot{V}\) in sleep (9).

However, there is some evidence to suggest that the fall in \(\dot{V}\) with sleep is not simply due to elevated UAR. For example, a correlation between the size of the change in UAR from wakefulness to sleep and the change in \(\dot{V}\) would be expected, but this has not been found (12). Also, an application of nasal continuous positive airway pressure to eliminate the rise in airway resistance in sleep does not eliminate the rise in end-tidal PCO₂ (PETCO₂) in nonsnoring subjects (16). In subjects with a permanent tracheostomy, UAR does not rise with sleep, but PETCO₂ is elevated and \(\dot{V}\) is lowered in non-rapid-eye-movement sleep compared with wakefulness to the same degree as it is in normal age-matched subjects (17). Factors responsible for the fall in \(\dot{V}\) during sleep could include an increased ventilatory threshold to PCO₂. In mechanically ventilated subjects, it has been shown that the increase in PCO₂ with sleep is in part due to a higher CO₂ threshold for recruitment of the Di; thus, for a particular level of PCO₂, there is reduced drive to the respiratory muscles in sleep compared with wakefulness (21). This altered response to CO₂ can be regarded as a manifestation of the wakefulness stimulus, but it is also possible that the wakefulness exerts its influence by direct input to motor neurons in the brain stem respiratory center. When 10 cmH₂O of inspiratory positive airway pressure were applied to spontaneously breathing and sleeping subjects, PETCO₂ remained constant, indicating that chemical reflexes were dominant in controlling \(\dot{V}\), whereas in wakefulness \(\dot{V}\) fell when inspiratory positive airway pressure was added, presumably because of a wakefulness factor. This finding has been regarded as indirect evidence of a wakefulness drive to breathe (18).

If withdrawal of the wakefulness stimulus to breathe is responsible for the sleep-related fall in \(\dot{V}\), then changes in \(\dot{V}\) would be expected to coincide with shifts between wakefulness and sleep. With the use of breath-by-breath analyses during the sleep-onset period, it has been shown that \(\dot{V}\) falls abruptly within one or two breaths of a change from \(\alpha\) to \(\theta\) (11, 12), but the UAR rise in sleep does not correspond to the fall in \(\dot{V}\). If sleep becomes established after an \(\alpha\) to \(\theta\) transition, \(\dot{V}\) falls only a little further before stabilizing, but UAR continues to rise until slow-wave sleep is established. Thus most of the fall in \(\dot{V}\) has occurred by the time non-rapid-eye-movement sleep is established, whereas the rise in UAR progressively increases into slow-wave sleep (13).

To summarize, a hypothesis that may explain the reduced \(\dot{V}\) in sleep is that there is a loss of drive to both the respiratory pump muscles and UA dilator muscles at sleep onset, resulting in an initial reduction in \(\dot{V}\) and rise in UAR. This fall in activity can be regarded as a withdrawal of the wakefulness stimulus to respiratory
drive. Chemical and other reflexes modify these changes as sleep progresses but not enough to return $V$ and UAR to awake values. This study is designed to assess the activities of two respiratory pump muscles, the Di and external intercostals (ICs), and of two UA muscles, genioglossus (GG) and tensor palatini (TP), at $\alpha$ to $\theta$ and $\theta$ to $\alpha$ transitions during the sleep-onset period.

### METHODS

#### Subjects

Eleven healthy men who were regular nighttime sleepers and who were nonsmokers and nonsnorers were studied. They were aged between 18 and 25 yr, and each had a body mass index $< 25$ kg/m$^2$. Each subject was studied for 2 nights separated by at least 1 wk. They were not specifically asked to be sleep deprived. The University of Melbourne Human Ethics Committee approved the study, and each subject gave written informed consent before the study commenced.

#### Laboratory Procedure

Subjects were asked not to consume alcohol or caffeine on the day of each study. They arrived in the sleep laboratory at 9:00 PM and, after having the monitoring equipment attached, went to bed at around 11:00 PM in a dark, quiet room. They maintained a supine posture throughout data collection. Initially, they were asked to remain awake for $\sim 10$ min before falling asleep so that baseline EEG activity could be recorded. To obtain multiple sleep onsets, they were woken once stable stage 2 sleep had been observed and then allowed to fall asleep again. This was repeated until $\sim 4$ h of data had been collected.

Sleep, electromyographic (EMG), and respiratory measurements were recorded with a 16-channel Grass polygraph (model 7D). Occipital EEG, all EMGs, airflow, and pressure measurements were also recorded on an IBM-compatible 486 personal computer. Central ($C_2/A_2$) and occipital ($O_1/A_2$) EEGs as well as an electrooculogram were recorded. For each subject, the occipital EEG activity during each breath was assessed as being predominantly $\alpha$ or $\theta$, as previously described (11). Briefly, for each subject, 10 min of unambiguous $\alpha$ and $\theta$ were identified visually. Automated period analysis, using peak-to-peak analysis with an amplitude criterion of 5 µV to define a peak, was used to calculate the ratio of each breath within these periods, and the signal-detection measurement, the equal likelihood ratio, was used to determine the value that best discriminated $\alpha$ from $\theta$ breaths. When this criterion ratio had been calculated for a particular subject, that subject’s occipital EEG was analyzed with the breath-by-breath automated period analysis. For each breath, a ratio of EEG activity $> 8$ Hz ($\alpha$) or $\leq 8$ Hz ($\theta$) was calculated. This ratio for each breath was classified as $\alpha$ or $\theta$ by comparison with the criterion ratio for that subject.

In addition, the sleep period was classified into three phases. Phase 1 was defined as the period from lights out to the first appearance of $\theta$ activity in which three of five consecutive breaths were classified as $\theta$. Phase 2 was defined as the period from the end of phase 1 to the first occurrence of a sleep spindle or K complex. Phase 3 was defined as the period from the end of phase 2 to the end of the onset. The development of sleep was described in terms of these phases rather than as stages of sleep, because the changes between phases can be identified more precisely in time than changes between stages, which are arbitrarily defined in terms of epochs extending over a period such as 30 s. Each breath could then be identified as occurring during phase 1, 2, or 3, and breaths within phases 2 and 3 could be identified as occurring during $\alpha$ or $\theta$ EEG activity.

#### EMG Recordings

Diaphragmatic EMG was recorded with gold-cupped surface electrodes placed anteriorly over the subcostal margin, and external IC EMG was recorded with surface electrodes placed laterally over the sixth intercostal space. Fine-wire intramuscular electrodes were used to record GG and TP EMGs. The wire was stainless steel 3/1,000-in. thick, with a 1/1,000-in. Teflon coating. The Teflon was stripped from the end of the wire for 1.5 mm, and a 1-mm hook was fashioned in the end of the wire. The wires were inserted into the muscles perorally with hypodermic needles. The sites of insertion were anesthetized with a small amount of 2% lidocaine gel. While the electrodes were being inserted the visual and auditory EMG signals were monitored to ensure that the electrodes were placed in muscle. To confirm that the electrodes were in the correct muscle, a series of maneuvers were performed that have previously been shown to elicit responses from GG and TP (14, 23). Jaw opening, jaw protrusion, blowing, sucking, swallowing, nasal breathing, and increased tidal volume produced increases in the EMG activity of TP. Tongue protrusion, the Muller maneuver, swallowing, and increased tidal volume produced increased EMG activity in GG.

#### Measurement of V

An oronasal mask with an air-filled cushion was strapped to the head tightly enough to eliminate any leaks. A heated pneumotachograph (Morgan) was attached to the mask. The dead space of the mask and pneumotachograph was $\sim 120$ ml. The pneumotachograph was connected to a differential pressure transducer (Validyne model DP45–14) and to a carrier demodulator (Validyne CD75), which converted the output to a voltage signal. Airflow was calibrated with a flowmeter (Sharot 1355). The airflow signal was analyzed off-line to calculate extrapolated minute $V$ for each breath.

#### Measurement of UAR

Simultaneous recordings of mask pressure, epiglottic pressure, and airflow were used to calculate UAR. Mask pressure was recorded via a pressure transducer (Validyne DP45–28) and carrier demodulator (Validyne CD15). The other side of the pressure transducer was connected to an equal length of tubing left open to the atmosphere. Epiglottic pressure was
measured with a transducer-tipped catheter (Millar model MPC-500) inserted through the nose and advanced until the tip was 1 cm below the base of the tongue. The nostril was premedicated with 0.05% oxymetazoline hydrochloride spray and 2% lidocaine gel. Computer software was used to calculate the pressure gradient across the UA from epiglottis to mask and to zero this pressure differential at the end of inspiration and at the end of expiration, the points of zero flow. Whereas a number of resistance measurements were generated by the software, the UAR reported was the resistance at peak airflow.

Data Analysis

Overall mean values for each phase and state. The mean V and UAR in phase 2, phase 2i, phase 3, and phase 3i were calculated within subjects by averaging all breaths of each type and then over subjects. For each subject, the mean EMG activities of the four muscles for each phase and state were expressed as a percentage of the average phase 1 activity for that subject. These data were then averaged across the subjects.

Changes at α to β and β to α transitions. 1) Once each breath had been classified as occurring during α or β EEG activity, computer software was used to identify sets of consecutive α or β breaths occurring on either side of α to β transitions and of β to α transitions. Thus, for each transition, four to ten breaths were identified, two to five consecutive α breaths and two to five consecutive β breaths. Each of these breaths then had an identifiable position within a transition from −5 to +5. For each subject, the parameters of interest were averaged for each breath position. These parameters were V, UAR at peak flow, and the EMG activities of Di, IC, GG, and TP muscles expressed as arbitrary units. Each subject had to have data from at least five breaths at a particular breath position for those data to be included, so that an aberrant breath from one subject would not unduly bias the group data.

2) As raw score EMG units are arbitrary and depend on degrees of amplification, group data can be excessively influenced by one subject, thus the EMG activity for each posttransition breath was expressed as a percentage of the pretransition baseline level. This baseline was defined as the average of the breaths −5 to −2 for each type of transition, i.e., α to β in phase 2, α to β in phase 3, β to α in phase 2, and β to α in phase 3. Breath position −1 was not used to determine the baseline, since a breath in the +1 or −1 position may have the change in EEG activity occurring within it and so it may not be purely α or β activity. It should be noted that because the EEG state transition did not typically occur at the onset of the inspiratory phase, there was a lack of precision in the classification of breaths at transitions results in some smoothing of the data over the transition, so that the impression is created that changes occurring at a transition are commencing before the actual transition occurs.

Extended transition data. Initially, only five breaths on either side of a transition were used so that a reasonable numbers of breaths and subjects were represented at each breath position. However, to see whether there were further changes in the EMG activities beyond the 5th posttransition breath, the α to β transitions were extended to 20 posttransition breaths. In this analysis, there only had to be one breath from each subject at each breath position for the data to be included, and the EMG activities were again expressed as a percentage of the mean activity of the −5 to −2 breaths. Data from phases 2 and 3 were combined.

Statistics

Overall mean data for each phase and state. A 2 × 2 ANOVA with repeated measures on each factor was used to assess the effect of phase and state on V, UAR, and EMG activities expressed as a percentage of phase 1 activity. In addition, one-sample t-tests were used to compare EMG activity in phase 2 and phase 3 with activity in phase 1.

Changes at transitions. For each transition type, single-sample t-tests were performed, comparing data at each posttransition breath position expressed as a percentage of the mean of the −5 to −2 data with a reference value of 100%.

Extended transitions. Single-sample t-tests were again performed, comparing data at each posttransition breath position expressed as a percentage of the mean of the −5 to −2 data with a reference value of 100%.

A P value < 0.05 was considered to be significant for all statistical analyses.

RESULTS

The data from one subject were discarded because the computer file was corrupted and the data could not be analyzed, and the data from another were discarded because he had frequent apneas. Thus the data from nine subjects, each completing 2 nights, were analyzed. An example of the raw data is shown in Fig. 1. It shows

Fig. 1. An example of raw data showing raw diaphragm (Di) EMG (EMGDi), raw intercostal (IC) EMG (EMGIC), raw tensor palatini (TP) EMG (EMGTP), raw genioglossus (GG) EMG (EMGGG), central EEG, electrooculogram (EOG), airflow (V), and Millar pressure (P) signals.
changes in the EEG activity from \( \alpha \) to \( \theta \) and then from \( \theta \) to \( \alpha \), and the associated falls and rises in \( V \) and EMG activities of Di, IC, GG, and TP. The ECG signal can be seen in the raw Di and IC EMG tracings. Note that the changes in the EMG activities coincide very closely with the changes in the EEG.

Overall Mean Values for Each Phase and State

The group mean data as a function of state (\( \alpha \) and \( \theta \)) and phase (2 and 3) for all breaths for \( V \), UAR at peak flow, and the activities of the muscles expressed as a percentage of phase 1 activity are shown in Table 1. \( V \) was significantly lower in \( \theta \) than in \( \alpha \) in both phases 2 and 3. UAR was greater in \( \theta \) than in \( \alpha \) in both phases 2 and 3 (Table 1). Di total inspiratory activity and phasic activity were lower in sleep (\( \theta \)) compared with wakefulness (\( \alpha \)), but there was no difference in tonic activity. IC and GG total inspiratory, phasic, and tonic activities were not significantly different between sleep and wakefulness. TP total inspiratory, phasic, and tonic activities were greater in wakefulness than in sleep. With respect to phase, Di and GG total inspiratory activities and phasic activities were higher in phase 3 than in phase 2. There were no differences in their tonic activities between the phases. IC and TP total inspiratory, phasic, and tonic activities were not significantly different between phases 2 and 3. There were no significant state-by-phase interactions.

A comparison of \( \alpha \) values in phases 1, 2, and 3, expressed as a percentage of phase 1 activity, indicated that Di total inspiratory and phasic activities and GG total inspiratory and phasic activities were all significantly greater in phase 3 than in phase 1. There were no other significant differences between phase 3 and phase 1 activities. There were no significant differences between phase 2 and phase 1 activities for any of the muscles.

Changes at Transitions

To examine the state changes in more detail, the group data for each of the five breaths on either side of transitions were plotted. There was an average of seven sleep onsets per night (range 3–13). The mean number of transitions per subject were 55.0 (range 3–13). The mean number of transitions per night (range 0–180), 43.6 (range 0–180), 43.6 \( \theta \) to \( \alpha \) transitions in phase 2 (range 13–93), and 58.0 \( \theta \) to \( \alpha \) transitions in phase 3 (range 0–146). The data for total inspiratory EMG activity are illustrated in Figs. 2 and 3, for phasic activity in Figs. 4 and 5, and for tonic activity in Figs. 6 and 7. Significant effects have been indicated on the graphs.

\( V \) fell and UAR increased at \( \alpha \) to \( \theta \) transitions and \( V \) rose again and UAR fell at \( \theta \) to \( \alpha \) transitions. The changes were greater in phase 3 than in phase 2. Di total inspiratory activity fell at \( \alpha \) to \( \theta \) transitions, with a greater fall in phase 3. Phasic activity also fell, but there was no significant change in tonic activity. At \( \theta \) to \( \alpha \) transitions, Di total inspiratory and phasic activities increased, more so in phase 3 than in phase 2.

IC total inspiratory and phasic activity had inconsistent changes at \( \alpha \) to \( \theta \) transitions, and tonic activities did not change. At \( \theta \) to \( \alpha \) transitions, there were no significant changes.

GG total inspiratory and phasic inspiratory activity fell at \( \alpha \) to \( \theta \) transitions for one to three breaths but then returned to the baseline level. Tonic GG activity did not show a consistent fall. At \( \theta \) to \( \alpha \) transitions, GG total inspiratory, phasic, and tonic activities significantly increased on the first or second \( \alpha \) breath in phase 3, but not in phase 2.

Table 1. Group data for minute \( V \), UAR at peak flow, and EMG activity expressed as %phase 1 activity for Di, IC, GG, and TP

<table>
<thead>
<tr>
<th></th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Significance</th>
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<tbody>
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<td>( \alpha )</td>
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<td>( \theta )</td>
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Table 1. Group data for minute \( V \), UAR at peak flow, and EMG activity expressed as %phase 1 activity for Di, IC, GG, and TP

<table>
<thead>
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<th></th>
<th>( \alpha )</th>
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<tbody>
<tr>
<td>( \alpha )</td>
<td>10.3 ± 1.2</td>
<td>9.1 ± 1.1</td>
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<tr>
<td>( \theta )</td>
<td>10.9 ± 1.4</td>
<td>8.5 ± 1.1</td>
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EMG activity, %phase 1 activity

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<tr>
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<tr>
<td>( \alpha )</td>
<td>106.7 ± 22.1</td>
<td>95.4 ± 20.2</td>
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<tr>
<td>( \theta )</td>
<td>100.8 ± 27.1</td>
<td>94.1 ± 25.3</td>
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<tr>
<td>( \alpha )</td>
<td>92.4 ± 41.9</td>
<td>97.0 ± 43.8</td>
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<tr>
<td>( \theta )</td>
<td>109.8 ± 51.1</td>
<td>109.8 ± 52.1</td>
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<tr>
<td>( \alpha )</td>
<td>84.4 ± 37.2</td>
<td>87.4 ± 36.4</td>
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<tr>
<td>( \theta )</td>
<td>127.7 ± 47.9</td>
<td>154.9 ± 59.9</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>131.7 ± 61.1</td>
<td>157.6 ± 72.8</td>
</tr>
<tr>
<td>( \theta )</td>
<td>122.0 ± 43.3</td>
<td>146.2 ± 67.2</td>
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<tr>
<td>( \alpha )</td>
<td>192.2 ± 317.1</td>
<td>149.4 ± 234.6</td>
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<tr>
<td>( \theta )</td>
<td>179.5 ± 279.2</td>
<td>182.7 ± 186.9</td>
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Values are means ± SD. Data from all breaths are included. \( V \), ventilation; UAR, upper airway resistance; Di, diaphragm; IC, intercostal; GG, genioglossus; TP, tensor palatini; P, phase; S, state. Significance was set at \( P < 0.05 \).
TP total inspiratory, phasic, and tonic activities decreased in phase 2. The decreases in phase 3 were not significant because of one subject's data. In phase 3, the subject's TP EMG activity fell to very low levels when there was a long period of $\theta$, rose with $\alpha$ activity, and fell again when $\theta$ was resumed, consistent with other subjects' data, but took a while to fall to the very low levels. When an $\alpha$ to $\theta$ transition was spanned...
by a breath that was classified as occurring during \( \alpha \) activity, some of the very low TP EMG activity in the period of \( \theta \) preceding the transition was incorporated into the \( \alpha \) breath, so that the average \( \alpha \) TP activity for that breath was artificially low, distorting the pattern of change. When these data were excluded, the changes in phase 3 were significant. At \( \theta \) to \( \alpha \) transitions, TP total inspiratory and phasic activities...
increased, but there was no significant increase in tonic activity.

In summary, at transitions from $\alpha$ to $\theta$, there were decreases in the EMG activities of Di, IC, GG, and TP, although there were differences in duration over which activity was decreased. At transitions from $\theta$ to $\alpha$, there were increases in the activities of Di, GG, and TP.

**Extended Transitions**

The $\alpha$ to $\theta$ transition data for total inspiratory EMG activity were extended to 20 posttransition breaths; phases 2 and 3 were combined (Fig. 8). There was a significant fall in Di activity, although by the 17th posttransition breath its activity was no longer significantly below baseline. There was no significant change from baseline in IC. GG activity had an initial significant fall below baseline, although by the 4th posttransition breath it was no longer significantly below baseline and by the 15th breath it was significantly above baseline. TP activity fell below baseline immediately after the transition and was still significantly below baseline by the 20th posttransition breath.

**DISCUSSION**

This study illustrates several findings with respect to the activities of respiratory pump and UA muscles at sleep onset. The first was that both phasic Di activity and phasic and tonic TP activities were reduced in sleep compared with wakefulness. This conclusion only applies to the sleep-onset period during which our subjects were studied. Because the subjects were woken once stable sleep had become established, the results could not be applied to differences between stable sleep and wakefulness. The discrepancy between our study and others that have found Di activity to be higher, or the same, in sleep than in wakefulness (8, 22) is likely to be due to recruitment of the Di if sleep is allowed to progress undisturbed after the initial fall in Di activity at the transition from $\alpha$ to $\theta$. The TP findings are consistent with those of Wheatley et al. (27) and Tangel...
et al. (24), who found that TP activity was lower in stable sleep than in wakefulness. Other studies have shown that overall GG activity is the same in stable sleep as in stable wakefulness (23, 24, 30), which is consistent with our data.

The second and more important finding of this study relates to the detailed examination of the changes in respiratory muscles. This has shown that the phasic activities of all muscles decreased within a few breaths of a change from \( \alpha \) to \( \theta \) EEG activity and that the tonic activity of TP also decreased. Not only did GG activity fall abruptly but it had recruitment that occurred within five breaths of the transition, so that the level of GG activity in \( \theta \) was the same as in \( \alpha \). This is consistent with the idea that GG activity is important for maintaining a patent UA in sleep (24): if GG was not recruited during sleep, then UAR would rise further and the UA would be subject to collapse and, possibly, closure. We do not have data to explain the mechanism of recruitment of GG following its initial fall but, consistently with others, we speculate that GG is recruited in response to increasing negative UA pressure and/or rising CO\(_2\). The response of GG to negative UA pressure is delayed in sleep and is variable between studies and between subjects within studies (26). An increase in activity in response to CO\(_2\) has been shown in GG in humans (1), in GG in rabbits (2), and in the hypoglossal nerve in cats (3). In contrast to GG, TP activity did not recover over 20 breaths following a transition.

At \( \theta \) to \( \alpha \) transitions, there were abrupt increases in the activities of DI, IC, GG, and TP, particularly in phase 3. As these changes occurred within a few breaths of a change from \( \alpha \) to \( \theta \) and from \( \theta \) to \( \alpha \), it is likely that state had a direct influence on the activities of these muscles. This supports the notion of the wakefulness stimulus having a direct influence on the activities of respiratory muscles (both pump and UA) during wakefulness, so that, when it is withdrawn in sleep, respiratory muscle activity falls. Because the wakefulness stimulus returns with \( \alpha \) activity, the activities of these muscles increase. It is not possible in this study to determine how the wakefulness stimulus exerts its influence on
the respiratory muscles, but as discussed below it could be by altering the ventilatory sensitivity and/or set point to CO₂.

Mezzanotte et al. (15) is the only other group to study respiratory muscle changes at sleep onset. They found that in the first two breaths after the EEG changed to α, the GG EMG fell to 89.7 and 87.4% of the baseline activity, and TP EMG fell to 94.5 and 98.8%. These are comparable to the changes we found, although by analyzing 20 posttransition breaths we found that GG increased again after this fall and that TP activity continued to fall so that it was 75% of its pretransition level by the 5th posttransition breath, and 61% by the 20th breath. Our study also looked at θ to α transitions and showed brisk rises in Di, IC, GG, and TP activities with a return to α activity. We simultaneously measured V, UAR, and the EMG activities of Di and IC, demonstrating a fall in V and Di activity and rise in UAR at α to θ transitions. When a distinction is made between the phasic and tonic components of the respiratory muscles, it can be seen that at α to θ transitions phasic activity of Di and GG fell with little change in tonic activity. In contrast, TP had little change in phasic activity but a clear fall in tonic activity. This is consistent with White's proposition that GG is predominantly a phasic muscle and TP is predominantly a tonic muscle (29).

These data support the hypothesis that the reduced V seen at sleep onset is at least in part due to a fall in Di activity and is not solely a consequence of raised UAR. The data also indicate that the increase in UAR, which is initiated early in sleep onset, is a consequence of the fall in activity of the UA dilator muscles. It is likely that as sleep progresses phasic respiratory muscles such as Di are recruited (8, 22, 24), probably via chemical and UA reflexes. Phasic UA muscles such as GG are also recruited after an initial fall, but tonic UA muscles such as TP are not, and so UAR remains above awake levels. It is not well understood how the various UA muscles interact to maintain UA patency. However, it is quite likely that TP helps to maintain UA patency by decreasing UA collapsibility, even though in isolation it may

![Fig. 6. Group tonic EMG activities for Di, IC, GG, and TP at α to θ transitions. EMG data are expressed as %average activity in -5 to -2 breaths for each transition. Only data from 5 breaths just before and from 5 breaths just after each transition are included. Each subject had to have at least 5 data points at a particular breath position for his data to be included at that position. Vertical dotted lines mark EEG transitions from α to θ. EMG breaths marked by * are significantly different from 100% (single-sample t-test), P < 0.05.](http://jap.physiology.org/Downloadedfrom)

not be an active UA dilator. Thus $\dot{V}$ falls at sleep onset for two reasons: first, because of reduced activity of respiratory muscles, either because of a direct reduction in activation of these muscles or because of reduced sensitivity of chemoreflexes during sleep; and second, because of an increase in UAR, both because of reduced TP activity and because UA reflexes are diminished during sleep, contributing to the elevated UAR.

If the levels of muscle activity were simply switching up and down in association with changes in EEG activity between $\theta$ and $\alpha$, the changes in EMG activities at $\theta$ to $\alpha$ transitions would be expected to be of the same magnitude as the changes at $\alpha$ to $\theta$ transitions. However, the increase in EMG activity at $\theta$ to $\alpha$ transitions is greater than the fall at $\alpha$ to $\theta$ transitions, suggesting that other mechanisms are playing a role at $\theta$ to $\alpha$ transitions. One possibility is that there is an additional component specifically associated with arousal that occurs in association with a shift from $\theta$ to $\alpha$, and this produces an increase in activity beyond that just due to a state change. Another contributing factor may be a difference in the $\dot{V}$ response to chemical stimuli at $\alpha$ to $\theta$ and $\theta$ to $\alpha$ transitions. It is known that there is a reduced ventilatory response to CO$_2$ during sleep (28) and that respiratory effort occurs at a higher CO$_2$ threshold in sleep than in wakefulness (21). At $\alpha$ to $\theta$ transitions, there is a fall in chemoreceptor sensitivity in association with a relatively lower chemical drive in the period of wakefulness preceding the transition. At $\theta$ to $\alpha$ transitions, there is an increase in chemoreceptor sensitivity in association with a relatively higher chemical drive in the period of wakefulness preceding the transition. At $\theta$ to $\alpha$ transitions, there is an increase in chemoreceptor sensitivity, but this is associated with a greater chemical drive because of the increased Pco$_2$ and decreased Po$_2$ during sleep. Therefore, at $\theta$ to $\alpha$ transitions, the increase in chemoreceptor sensitivity produces a greater change in $\dot{V}$ because the baseline drive is higher, whereas the same degree of chemoreceptor drive change at $\alpha$ to $\theta$ transitions has a smaller effect as the baseline level of drive is lower. Either of these explanations or a combination of the two can explain the greater Di activity in phase 3$\alpha$ compared with phase 1$\alpha$.

The third finding of this study was that changes of pump muscle (Di and IC) activity differed between
Fig. 8. Group V̇, UAR, and total inspiratory EMG activities for Di, IC, GG, and TP at α to θ transitions. EMG data are expressed as %average activity in −5 to −2 breaths for each transition. Only data from 5 breaths just before and from 20 breaths just after each transition are included. Each subject had to have only 1 data point at a particular breath position for his data to be included at that position. Data from phases 2 and 3 were combined. Vertical dotted lines mark EEG transitions from α to θ. EMG breaths marked by * are significantly different from 100% (single-sample t-test), P < 0.05.
phases 2 and 3. The two phases were analyzed separately because previous work (10) has shown that V˙ and UAR have greater changes between α and θ in phase 3 than in phase 2. There is a number of explanations for this. 1) If the wakefulness stimulus is having a direct influence on respiratory motoneurons and if its withdrawal is incomplete during phase 2 and complete in phase 3, then the changes in muscle activity between α and θ would be greater in phase 3 than in phase 2. 2) The difference in response to chemoreceptor drive between α and θ is greater in phase 3 than in phase 2 (4), again, producing greater muscle changes in phase 3 than in phase 2. 3) The difference in chemoreceptor drive itself may be greater. 4) If there is an arousal complex producing greater muscle activity with shifts from θ to α, this arousal response may have a greater influence in phase 3. 5) There is also a methodological explanation. The periods of α between periods of θ tended to be longer in phase 2 than in phase 3, in which a period of α may only last for two or three breaths. Also, the periods of θ were generally briefer in phase 2 than in phase 3. This means that the five α breaths preceding an α to θ transition in phase 2 represented a more stable α, whereas the α breaths before an α to θ transition in phase 3 may have been the same α or arousal breaths that form part of the θ to α transition. Thus the pretransition activity was higher in phase 3 than in phase 2, at least in part explaining the trend to greater falls in Di activity at α to θ transitions in phase 3 than in phase 2.

Mezzanotte et al. (15) did not observe phasic TP activity in any of their eight normal subjects, whereas phasic TP activity was observed visually in all of our subjects in established sleep. One reason for the discrepancy with our study is the periods in which phasic activity is sought. Our subjects only showed evidence of phasic activity in TP after sleep had become established and the level of tonic activity had fallen considerably. We postulate that there is a low level of underlying phasic activity in TP, which is masked by the tonic activity during wakefulness and early sleep but which becomes apparent when the level of tonic activity falls to very low levels as sleep becomes established. Mezzanotte et al. (15) did not report data from their subjects in stable sleep so they did not have the same opportunity to observe phasic TP activity as we had.

It is not possible to draw any conclusions about the relative changes of the muscles at sleep onset because it is not possible to determine whether the neural input to each muscle is the same or whether the baseline EMG activities of different muscles are the same. Also, it is not possible to relate changes in EMGs with changes in UAR or V, as the relationship between EMG activities and the force generated by the muscles is not known. What was of importance was that the muscles change in the same direction as each other in association with changes in state.

The level of resting V in our subjects was high, most likely because of stimulation of oral and nasal mucosa by the Millar catheter (20). The differences in V that we observed were similar to those reported by others (6, 11–13, 19, 22, 25, 28, 30) and so are not simply explained by voluntary hyperventilation in our subjects. A fall in V with sleep has also been demonstrated with impedance plethysmography (32) and magnetometers (7, 27), and so it was not specifically related to the instrumentation we used. Also, the changes at the transitions that we observed were too abrupt to be explained by changes in CO2 levels.

There are two other technical points. 1) It is possible that the surface Di electrodes were not recording pure Di activity; however, we believed that the main aim of the study could not justify the use of intramuscular or esophageal Di electrodes, since we were interested in the Di as a representative pump muscle rather than as a discrete muscle by itself. 2) We chose to record from the external ICs rather than from the parasternal ICs because, as the external IC muscles are less active than the parasternal ICs during quiet respiration, if there was an increase in activity at α to θ transitions, it would be more likely to be observed.

In summary, we have shown that during the sleep-onset period phasic activity of Di, IC, and GG and phasic and tonic activities of TP fell within a few breaths of a change from α to θ and that there was recruitment of GG after the initial fall but no recruitment of TP for at least 20 breaths. With changes from θ to α, the phasic and tonic activities of Di, GG, and TP increased. It was concluded that the fall in V at sleep onset is a direct consequence of both the reduction in activities of the respiratory pump and UA muscles with sleep.

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