Swallowing function and upper airway sensation in obstructive sleep apnea

Vincent Jobin, Victoria Champagne, Josée Beauregard, Isabelle Charbonneau, David H. McFarland, and R. John Kimoff

Respiratory Division and Sleep Laboratory, Meakins-Christie Laboratories, McGill University Health Centre, and Department of Respiratory Medicine, Hôtel-Dieu de Montréal, and Department of Speech and Audiology, University of Montreal, Montreal, Quebec, Canada

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J Appl Physiol 102: 1587–1594, 2007. First published December 21, 2006; doi:10.1152/japplphysiol.00439.2006.—The objective of this study was to determine whether impaired upper airway (UA) mucosal sensation contributes to altered swallowing function in obstructive sleep apnea (OSA). We determined UA two-point discrimination threshold (2PDT) and vibratory sensation threshold (VST) in 15 men with untreated OSA and 9 nonapneic controls (CL). We then assessed swallowing responses to oropharyngeal fluid boluses delivered via a catheter. The threshold volume required to provoke swallowing and the mean latency to swallowing were determined, as was the phase of the respiratory cycle in which swallowing occurred [expressed as percentage of control cycle duration (%CCD)] and the extent of prolongation of the respiratory cycle after swallowing [inspiratory suppression time (IST)]. 2PDT and VST were significantly impaired in OSA patients compared with CL subjects. 2PDT was positively correlated with swallowing latency and threshold volume in CL subjects, but not in OSA patients. Threshold volume did not differ between the groups [median value = 0.1 ml (95% confidence interval = 0.1–0.2) for OSA and 0.15 ml (95% confidence interval = 0.1–0.16) for CL], whereas swallowing latency was shorter for OSA patients [3.3 (SD 0.7) vs. 3.9 (SD 0.8) s, P = 0.04]. %CCD and IST were similar for OSA patients and CL subjects. However, among OSA patients there was a significant inverse relation between VST and IST. These findings suggest that oropharyngeal sensory impairment in OSA (6, 13). More recently, we demonstrated that sensation is also impaired in the velopharynx and larynx and that, in patients with abnormal sensation, the severity of impairment correlated with OSA severity (21). These observations raise the possibility that a UA mucosal sensory defect could contribute to altered afferent control of UA function in OSA (6, 12, 13, 16, 21) and may therefore represent a pathophysiological factor contributing to UA collapse during sleep.

Recent studies have suggested that OSA patients may have abnormal swallowing function. In video-radiographic studies, Jaghagen et al. showed abnormalities of solid and liquid bolus handling in snorers (15) and patients with OSA (14). Teramoto and co-workers (28) reported prolonged latency to swallowing after an oropharyngeal fluid bolus in OSA patients compared with normal subjects (28). These changes were found to correlate with the severity of nocturnal hypoxemia (27).

Swallowing is initiated and regulated by neural afferents in the oropharynx and laryngeal mucosa (10, 19). These afferents interact with a central pattern generator, which produces the stereotyped patterned activity in swallowing and respiratory musculature necessary for food or liquid transport and airway protection. Swallowing must be coordinated with respiration, since both share a common passageway, and aspiration must be prevented. To ensure normal coordination, complex interrelations exist between the two central pattern generators that regulate breathing and swallowing at the brain stem level (4, 10, 11). Swallowing occurs almost exclusively during late expiration in seated humans and is accompanied by respiratory inhibition and other processes, such as vocal cord closure and laryngeal elevation, that assist in protecting the laryngeal aperture (10, 17). Although specific and common afferent pathways are not well described for the initiation of swallows and the reflexes that determine UA patency, they clearly share similar neuromuscular structures within the UA (19).

Recent work in our laboratory demonstrated a selective impairment of mucosal sensory function in the UA of OSA patients (16). Specifically, we found that vibratory sensation and two-point discrimination were impaired in the oropharynx, but not at control sites on the lip and hand, in OSA patients and snorers compared with a group of nonsnoring control subjects. Other groups subsequently corroborated the presence of an oropharyngeal sensory impairment in OSA (6, 13). More recently, we demonstrated that sensation is also impaired in the velopharynx and larynx and that, in patients with abnormal sensation, the severity of impairment correlated with OSA severity (21). These observations raise the possibility that a UA mucosal sensory defect could contribute to altered afferent control of UA function in OSA (6, 12, 13, 16, 21) and may therefore represent a pathophysiological factor contributing to UA collapse during sleep.

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Thus alterations of swallowing function in OSA patients could reflect a problem of afferent neural input from UA structures, altered central integrated control of UA function, efferent neuromuscular dysfunction, or a combination of these factors. Elucidation of altered swallowing mechanisms in OSA could potentially provide insights into the peripheral and central mechanisms that contribute to the pathophysiology of UA dysfunction in OSA.
In the present study, we hypothesized that UA mucosal sensory impairment in an OSA patient would correlate with alterations in swallowing function. The specific aim was to assess swallowing function in OSA patients compared with age- and sex-matched nonapneic, nonsnoring control subjects and evaluate the relations between measures of UA sensation and swallowing reflex responses and respiratory-swallowing interactions in these two groups.

**METHODS**

**Study Population**

OSA patients were recruited from the Sleep Disorders Clinic of the Royal Victoria Hospital, and control (CL) subjects were recruited through local advertisements. The Human Ethics Committees of the Royal Victoria Hospital approved the study protocol. All subjects provided written informed consent. OSA patients were ≥18-yr-old untreated men with a history of snoring and symptoms compatible with sleep apnea and an apnea-hypopnea index (AHI) of >15 events per hour during overnight diagnostic polysomnography. CL subjects were similar-aged men with a history of only rare or no snoring, no other symptoms of sleep apnea, and a respiratory disturbance index of <10 events per hour and snoring for <20% of the night on a home recording with an Edentrace II recorder (24).

Exclusion criteria for all subjects included any previous treatment for snoring or OSA, previous UA surgery (excluding remote tonsillectomy), previous cerebrovascular accident, diabetes, any neuropathy or active neurological disease, or other swallowing complaint. Other exclusion criteria included recent upper respiratory tract infection, excessive gag reflex or difficulty accessing the oral cavity for sensory testing due to anatomic constraint, and use of medications that could potentially interfere with sensory or reflex testing.

**Sleep Recordings**

**Polysomnography.** Overnight polysomnography included recording of standard electroencephalographic leads (C4-A1/C3-A2), bilateral electrooculogram, chin and anterior tibialis electromyograms, airflow via nasal pressure cannula (15), thoracoabdominal movements via inductive plethysmography (Respirtrac Systems, Ardsley, NY) or piezo bands (EPM Systems, Midlothian VA), body position via infrared video and/or position sensor (EPM Systems), sound via a microphone suspended above the subject’s head, and arterial oxyhemoglobin saturation (SaO₂) via finger pulse oximetry (Biox 3700, Ohmeda, Boulder, CO). All signals were acquired on a digital data management system (Sandman, Mallinkrodt, Ottawa, ON, Canada). Studies were scored manually by trained, experienced polysomnographic technologists with expert physician review. Sleep-wake state was defined according to standard criteria (23). Snoring was identified as typical inspiratory bursts of activity on the microphone channel. Segments of snoring (≥2 consecutive snoring breaths) were tagged in the analysis software, with total snoring time calculated as the sum length of snoring tags. An obstructive apnea was defined as a ≥10-s episode of cessation of airflow with persistent respiratory effort and a hypopnea as a discrete episode of reduction in airflow or inspiratory flow limitation on the nasal cannula pressure signal (20) lasting >10 s with associated desaturation of >2% or arousal defined according to standard criteria (1). Apnea severity measures derived from the polysomnographic analysis included total number of apneas and hypopneas, apnea index (number per hour of sleep), hypopnea index, AHI, mean apnea and hypopnea duration, mean end-apneic SaO₂, nadir SaO₂ for the entire night, mean nocturnal SaO₂, and percentage of sleep with <90% SaO₂.

**Edentrace.** The data from Edentrace II, which include thermistor airflow, SaO₂, respiratory effort via ECG electrode impedance, heart rate, body position, and snoring via tracheal microphone, were downloaded to a personal computer and scored manually using the same Sandman analysis software used for polysomnography. Snoring was assessed as described above (see Polysomnography). Scoring criteria for respiratory events were similar to those used during polysomnography, except hypopneas were scored only when there was a ≥50% reduction in flow with ≥2% desaturation. The analysis of respiratory variables was similar to that for polysomnography, except AHI was calculated per hour of recording, rather than per hour of sleep.

**Experimental Protocol**

Sensory testing and the swallowing function assessment were carried out during the same session in the afternoon or early evening, within 4 wk of the diagnostic sleep recording. Subjects were studied awake, blindfolded, and in the seated position. Maintenance of wakefulness was confirmed continuously throughout the testing procedure by verbal interaction with the patient/subject and assessment of responses during testing. Testing of two-point discrimination threshold (2PDT) and vibratory sensation threshold (VST) was performed in random order in the UA and at two control sites (lower lip and hand).

Swallowing function was assessed after the sensory testing. Subjects were told that their swallowing function was being assessed, but they were not instructed to refrain from or favor swallowing otherwise. Swallowing responses were assessed using a provocation test consisting of infusion of a water bolus of known volume (see below).

**Sensory measurements.** UA mucosal sensation was tested using our previously established techniques (16). Briefly, 2PDT was measured using a series of two-point probes with fixed interprobe distances in the oropharynx along the margin of the soft palate lateral to the uvula on the right and left sides (mean value of the 2 sides is reported), as well as at control sites on the dorsum of the hand and on the lower lip. The largest interprobe distance in the oropharynx was 14 mm (16). Subjects who were unable to correctly identify 1 vs. 2 points, even at the largest interprobe distance, in the UA were assigned a threshold value of 14 mm.

VST was also determined as previously described (16) in the oropharynx on the upper portion of the anterior tonsillar pillar just below the palatal arch on the right and left sides (mean value of the 2 sides is reported), as well as at control sites on the fingertip and hand.

**Instrumentation for assessment of swallowing function.** After assessment of sensory responses, the subjects were instrumented with a water-filled nasopharyngeal catheter (2.7 mm diameter), positioned just below the palatal arch as visualized perorally, for administration of fluid boluses (7, 25, 26). The catheter was connected to a pressure transducer (Transpac) to provide the technician with a real-time display of the pressure traces and time to ensure bolus infusion at a constant rate. The infusion bolus was delivered manually through a standard 1-ml tuberculin syringe attached to the infusion catheter containing a continuous column of water. In our analysis, we confirmed the infusion catheter pressure trace that the fluid bolus infusion rate was similar in the two groups: median = 0.10 ml/s (95% confidence interval [CI]) = 0.06–0.72) vs. 0.11 ml/s (95% CI = 0.06–0.16) in OSA and CL, respectively (P = 0.93).

Pharyngeal pressure was measured with a second pressure transducer-tipped catheter (Gaeltec, Dunvegan, Scotland), which was placed in the oropharynx, with its tip located 2 cm distal to the infusion catheter. Pharyngeal pressure served as the primary swallowing marker (26). The position of the catheters was reassessed periodically during testing to ensure that no migration occurred due to swallowing or other movement. Viscous lidocaine (0.5 ml, 2% solution) was applied in one nostril before insertion of the catheters to facilitate passage of the catheter and minimize discomfort during placement. Swallowing assessment was begun ≥20 min after initial catheter placement to avoid any minor pharyngeal anesthetic effect that might have resulted from the small amount of viscous solution applied intranasally. A mercury strain gauge was placed around the
neck at the level of the thyroid prominence to detect laryngeal movement as an ancillary swallowing marker (17, 26). However, because key outcome measures were similar using either measurement, the pharyngeal deflection was used as the primary swallowing marker in the analysis. Breathing was monitored by thoracic and abdominal inductance plethysmography belts (Respiritrace). All signals (pharyngeal catheter, infusion catheter, mercury strain gauge, and inductance plethysmography) were sampled at 100 Hz, stored online, and visualized using the CODAS acquisition system (DATAQ Instruments, Akron, OH).

Protocol for assessment of swallowing function. After instrumentation, signals were recorded during 10 min of quiet breathing to assess baseline respiratory frequency and spontaneous swallowing. Swallowing provocation testing, which consisted of infusing boluses of water (ambient temperature) via the nasopharyngeal catheter at a constant rate (0.1 ml/s) during expiration, was then carried out to detect the patient's/subject's swallowing response to that stimulus. Infusions were separated by at least three respiratory cycles without intervening swallows. The initial infusion volume of 0.05 ml was followed by 0.05-ml increments up to a maximum of 0.30 ml. A minimum of 10 infusions were administered for each volume.

Swallows were detected as a positive deflection on the pharyngeal catheter trace (Fig. 1). Infusion time and infusion rate were calculated by dividing the volume infused by total infusion time. We analyzed only those swallow events that occurred within the respiratory cycle following the cycle in which the swallow occurred was then marked with a cursor. The entire cycle length, as well as the length of the inspiratory and expiratory phases, was measured for the perturbed and template control cycles. The phase of the respiratory cycle in which the swallow occurred was then determined, and the time between the start of the perturbed cycle and the swallow was expressed as a percentage of the control cycle duration (%CCD) (17, 18). We also determined the proportion of swallows that occurred during inspiration.

The respiratory-swallowing interaction was also assessed during swallowing provocation by measurement of the inspiratory suppression time (IST), defined as the time between the termination of swallowing and the start of the next inspiration (10) (Fig. 1). The values are those for all induced swallows at the threshold volume.

Statistical Analysis

Values for VST and swallowing latency were compared between the two experimental groups using Student’s t-test. Values for 2PDT and threshold volume were nonnormally distributed and were compared using the Mann-Whitney rank-sum test. Other variables are reported as means (SD). Swallowing latency between OSA patients and CL subjects at different bolus volume was compared by analysis of covariance. Correlations were determined between sensory threshold values and swallowing values, as well as with anthropometric data and OSA severity measures (16, 21) from the diagnostic polysomnogram, using Spearman’s rank correlation for 2PDT and threshold volume and Pearson’s product-moment correlation for VST and swallowing latency. Differences in %CCD, IST, and proportion of inspiratory swallows between OSA patients and CL subjects were compared using a t-test. Values are means (SD) (normally distributed) or median and 95% CI. A threshold of P < 0.05 was used for statistical significance.

RESULTS

Subject Characteristics

The characteristics of the study population are presented in Table 1. The mean age of the groups was similar, while body mass index was slightly, but significantly, higher for OSA patients than for CL subjects.

Sensory Testing

The values for sensory thresholds at the UA and control sites in the two experimental groups are shown in Table 2. Values for 2PDT were nonnormally distributed, and medians are shown, whereas VST values were normally distributed and means are shown (see above). The median values for 2PDT were not significantly different between the two experimental groups at the hand and lip control sites. However, a significant impairment of 2PDT was observed in the oropharynx of OSA patients compared with CL subjects. As for 2PDT, mean VST values were not significantly different between the two exper-

<table>
<thead>
<tr>
<th>Table 1. Subject characteristics</th>
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<tr>
<td></td>
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<tr>
<td>Name</td>
</tr>
<tr>
<td>Age, yr</td>
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<tr>
<td>BMI, kg/m²</td>
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<tr>
<td>AHI, events/h</td>
</tr>
<tr>
<td>OSA (n = 15)</td>
</tr>
<tr>
<td>44.2 (9.8)</td>
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<tr>
<td>32.4 (5.5)*</td>
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<tr>
<td>56.7 (28.5)*</td>
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<tr>
<td>CL (n = 9)</td>
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<tr>
<td>43.2 (14.7)</td>
</tr>
<tr>
<td>26.4 (2.7)</td>
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<tr>
<td>5.6 (3.5)</td>
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</tbody>
</table>

Values are means (SD). BMI, body mass index; AHI, apnea-hypopnea index; OSA, obstructive sleep apnea; CL, control. *P < 0.05 vs. CL.
imental groups at the finger and lower lip control sites, whereas values were substantially higher in the oropharynx of OSA patients than CL subjects. These findings are therefore consistent with our previous findings (16) and demonstrate a selective impairment of UA sensory function between OSA patients and CL subjects.

Swallowing Responses

The threshold volume required to precipitate swallowing was similar for the two groups (Fig. 2A). The median values for threshold volume were not significantly different: 0.10 ml (CI = 0.10–0.20) and 0.15 ml (CI = 0.10–0.16) in OSA and CL, respectively (P = 0.86).

OSA patients demonstrated a slightly, but significantly, shorter mean swallowing latency than CL subjects [3.29 (SD 0.71) vs. 3.94 (SD 0.83) s, P = 0.04] at the threshold volume (Fig. 2B). Furthermore, the swallowing latency-infusion volume relation was significantly different between OSA patients and CL subjects across infusion volumes (P = 0.0004, analysis of covariance; Fig. 3).

The respiratory-swallowing interaction data are shown in Table 3. Respiratory timing during quiet breathing was closely comparable between the two groups. Furthermore, baseline swallowing frequencies during instrumentation over the first 10 min of the experiment before administration of fluid bolus infusions were similar. OSA patients and CL subjects consistently swallowed in late expiration, with only a minority of swallows during inspiration.

When data are expressed as %CCD, swallows occurred slightly earlier in OSA patients than in CL subjects (Table 3). This pattern was observed when the swallow response occurred within the same respiratory cycle as the infusion or in the following cycle. This difference for swallows within the same cycle was statistically significant.

The prolongation of the respiratory cycle after swallowing expressed as the IST was not significantly different between OSA patients and CL subjects. No significant correlations were found between swallowing measures and any of the apnea severity measures described in METHODS for CL subjects or OSA patients.

There was a nonsignificant trend to a negative correlation between VST and %CCD for OSA patients (r = −0.32, P = 0.24), but not for CL subjects. However, there was a significant

Table 2. Sensory detection thresholds

<table>
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<tr>
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<th>OSA (n = 15)</th>
<th>CL (n = 9)</th>
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<tbody>
<tr>
<td>2 PDT, mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>20.0 (18–23)</td>
<td>20.0 (18–23)</td>
</tr>
<tr>
<td>Lip</td>
<td>3.0 (2.0–4.0)</td>
<td>3.0 (2.0–4.2)</td>
</tr>
<tr>
<td>UA</td>
<td>14.0 (13.5–14.0)*</td>
<td>12.5 (9.4–13.6)</td>
</tr>
<tr>
<td>VST, vibration units</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>1.5 (0.8)</td>
<td>1.0 (0.3)</td>
</tr>
<tr>
<td>Lip</td>
<td>1.7 (0.4)</td>
<td>1.8 (0.9)</td>
</tr>
<tr>
<td>UA</td>
<td>4.2 (1.0)*</td>
<td>2.0 (1.2)</td>
</tr>
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</table>

Values are medians (95% confidence interval) for 2-point detection threshold (2 PDT) and means (SD) for vibratory sensation threshold (VST). UA, upper airway. *P<0.05 vs. CL.
negative correlation between UA VST and IST for OSA patients (r = -0.52, P = 0.04; Fig. 5): the more severe the degree of sensory impairment, the less marked the prolongation of the respiratory cycle after the swallowing response. This relation was not observed for UA 2PDT, although the sensitivity of that analysis may have been hampered by the fact that most OSA patients demonstrated the maximum plateau value of 14 mm for 2PDT in the oropharynx (16). VST values for CL subjects are also shown in Fig. 4. There was no significant correlation for CL subjects (r = -0.34, P = 0.37).

**DISCUSSION**

In this study, we again demonstrated the presence of a selective impairment of oropharyngeal mucosal sensory function in OSA patients compared with CL subjects (16). However, we found no significant difference between OSA patients and CL subjects in the threshold volumes required to elicit a swallowing response but did find a slight, but statistically significant, reduction of the latency to swallowing responses in OSA patients. The analysis of respiratory-swallowing interactions showed that swallow responses tended to occur slightly earlier in the expiratory phase of the respiratory cycle in OSA patients but that changes in cycle length after swallowing were similar in the two groups.

Assessment of the relations between sensory and swallowing measures demonstrated a significant positive correlation between 2PDT (and a trend for VST) values and swallowing latency and threshold volume for CL subjects. There was no significant correlation of these variables for OSA patients, although the sensitivity of correlation analyses for 2PDT may have been limited by the maximal value of 14 mm observed in 10 of the 15 OSA patients, as previously discussed (16). However, we did observe a significant inverse correlation between the degree of UA sensory impairment (VST) and the extent of prolongation of the respiratory cycle after swallowing (IST) for OSA patients, but not for CL subjects.

Altered swallowing function in OSA could be due to changes in afferent neural input from UA structures, altered central integration of UA function, efferent neuromuscular dysfunction, or a combination of these factors. In this study, we postulated that an impairment of UA afferent neural input could impact the swallowing reflex response and the central integration of respiration and swallowing.

Although we hypothesized that the mucosal sensory impairment in OSA patients would be associated with increased threshold volume and swallowing latency, we found no increase in threshold volume and a mild reduction in latency

**Table 3. Respiratory-swallowing interactions**

<table>
<thead>
<tr>
<th></th>
<th>OSA (n = 15)</th>
<th>CL (n = 9)</th>
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<tbody>
<tr>
<td>TT, s</td>
<td>5.4 (0.8)</td>
<td>5.0 (0.8)</td>
</tr>
<tr>
<td>TI, s</td>
<td>1.4 (0.1)</td>
<td>1.4 (0.3)</td>
</tr>
<tr>
<td>TE, s</td>
<td>3.7 (0.7)</td>
<td>3.7 (0.6)</td>
</tr>
<tr>
<td>%CCD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>85.6 (11.3)</td>
<td>91.6 (19.9)</td>
</tr>
<tr>
<td>Same</td>
<td>111.6 (16.1)</td>
<td>134.7 (17.9)*</td>
</tr>
<tr>
<td>Next</td>
<td>62.9 (12.4)</td>
<td>71.5 (10.4)</td>
</tr>
<tr>
<td>IST, s</td>
<td>1.71 (0.51)</td>
<td>1.72 (0.83)</td>
</tr>
<tr>
<td>Inspiratory swallows, %</td>
<td>4.7</td>
<td>2.5</td>
</tr>
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</table>

Values are means (SD). TT, total respiratory cycle length; Ti, inspiratory period length; Te, expiratory period length; %CCD, percentage of control cycle duration; overall, %CCD for all induced swallows; same, %CCD for all swallows that occurred in the same expiration in which infusion was given; next, %CCD for all swallows that occurred in the respiratory cycle that followed the infusion; IST, inspiratory suppression time. *P < 0.05 vs. CL.
values (Figs. 2 and 3). These findings differ from those of Teramoto and colleagues (28), who reported significantly greater threshold volume and longer swallowing latency and shorter IST for their OSA patients than for their control subjects. Our OSA patients were younger, more obese, and of different ethnicity (Caucasian vs. Japanese) and suffered from more severe OSA (mean AHI = 57 vs. 20) (28). Thus differences in the duration and/or severity of disease, relative size and configuration of the UA, relative contribution of neuropathic mechanisms, or genetic differences in compensatory mechanisms might have accounted in part for the differences in our findings.

There were also several methodological differences between the two studies. Teramoto et al. (28) studied their patients in the supine position, rather than in the seated position, although there is considerable evidence that swallowing responses in the supine position are not different from those in the upright position. Shaker et al. (25) reported no difference in fluid bolus-induced swallowing latency in the seated vs. supine positions across a range of subject ages, and Barkmeier et al. (3) reported similar findings. One potentially important difference, however, was that Teramoto et al. recorded the “volume of water injected as a pressure difference by a pressure transducer,” while we directly measured the volume injected. Teramoto et al. reported injecting volumes of 0.4–2.0 ml, with all controls responding to 0.4 ml, but most OSA patients requiring ≥0.8 ml, whereas we injected 0.05–0.25 ml (over a similar time of 1–2 s), with all subjects responding to ≤0.25 ml. Furthermore, among our CL subjects and OSA patients, >0.3 ml invariably provoked uncomfortable cough and choking, in addition to swallowing. This discrepancy in volume tolerance may have been due to slightly different catheter placement [“suprapharyngeal” (28) vs. within the oropharynx adjacent to sensory testing sites], in that we previously showed that velopharyngeal sensory thresholds are higher than oropharyngeal values (21). Alternatively, the calibration of their indirect method for measurement of injected bolus volume (28) conceivably could have been problematic, or their subjects may have been markedly less sensitive to pharyngeal fluid stimuli. Unfortunately, Teramoto et al. did not evaluate UA sensation in their subjects, so the two studies cannot be compared in this regard.

Jaghagen et al. (14, 15) used video radiography to study swallowing of barium boluses in snorers and OSA patients. They reported that 43–61% of snorers and mild- and severe-OSA patients demonstrated swallowing abnormalities that were seen in only 7% of nonsnorers controls (14). These abnormalities were characterized as premature bolus leakage, i.e., penetration of the bolus into the hypopharynx and perilarynx without an elicited swallowing response; the presence of a residual bolus in the hypopharynx after swallowing; and, in a small number of subjects, penetration of the bolus into the larynx, although without frank aspiration. Premature leakage of the bolus from the pharynx without elicited swallowing is consistent with an impairment of pharyngeal sensation, although sensory function was not tested in that study (14).

The observation of swallowing changes in the larynx (14) is of interest, in that we recently demonstrated a mucosal sensory impairment in the larynx, as well as the oropharynx, using endoscopic air pressure pulse testing (21). The laryngeal sensory impairment was directly correlated with an impairment of the protective laryngeal adductor reflex and apnea severity (21). Swallowing function was not assessed in those patients, but other previous work supports a link between impaired laryngeal sensation and aspiration risk in dysphagia patients (2). Thus the laryngeal sensory impairment in OSA might contribute to the laryngeal swallowing changes described by Jaghagen et al. (14), although this remains to be directly tested.

Previous animal and human studies indicate that although laryngeal afferents contribute, oropharyngeal structures, including the tonsillar pillars, palatal margin, and posterior pharyngeal wall, convey sensory information that modulates swallowing responses (19). Although most afferents are facilitatory for swallowing, there appears to be a balance of modulating inputs, in that there are also clearly described inhibitory inputs to swallowing (19). Sensitivity to swallowing is also dependent on the physicochemical nature of the stimulus, such that relative responses to mechanical vs. water stimuli may differ at a given site (e.g., mechanical sensitivity is greater in the oropharynx, whereas water sensitivity may be greater at the larynx) (19).

In the present study, we observed positive correlations between sensory threshold values (significant for 2PDT, trend for VST) and swallowing latency and threshold volume for CL subjects (Fig. 4). This suggests that the specific receptors (location and receptor subtype) tested by our sensory techniques are directly involved in facilitating swallowing responses in CL subjects or that their function is reflective of the

Fig. 5. Individual values for IST vs. VST (vibration units). Degree of respiratory cycle prolongation demonstrated a significant inverse relation to severity of upper airway sensory impairment for OSA patients.
general sensitivity of other receptors that facilitate swallowing. On the basis of the findings in CL subjects, it was surprising that although pharyngeal sensation was impaired in OSA patients, the threshold volume to evoke a swallowing response was unchanged from that in CL subjects, swallowing latency was mildly, but significantly, reduced (Figs. 2 and 3), and there was no correlation between sensory threshold values and swallowing threshold and latency.

From the perspective of integrated afferent modulation of swallowing responses, the shortened swallowing latency suggests that the mucosal sensory changes in OSA lead to a net loss of inhibitory modulating influences on swallowing. This could be due to a loss of an inhibitory effect of mechanoreceptors. As noted above, facilitatory and inhibitory mechanoreceptor inputs to swallowing have been described previously (19). We previously showed that topical UA anesthesia increases inspiratory efforts during obstructive apneas, indicating an inhibitory effect on respiratory centers of some UA mechanoreceptors (5). As well, nasal continuous positive airway pressure has been shown to inhibit swallowing responses to fluid infusion (22), which is likely to be mediated by stimulation of UA receptors (although bronchopulmonary receptors could contribute). Thus attenuation of oropharyngeal sensory function may have preferentially affected these inhibitory afferents. Ebihara et al. (8, 9) reported that oropharyngeal application of capsaicin, which initially stimulates, but may subsequently desensitize, sensory receptors, shortens swallowing latency in dysphagia patients.

Alternatively, water-sensitive receptors may be affected differently by the processes leading to mucosal sensory impairment loss of mechanoreceptor sensitivity. Conceivably, the function of water-sensitive nerve endings could remain relatively unaffected or, in fact, be increased as part of a compensatory mechanism for the loss of mechanoreceptor sensitivity. This could therefore have contributed to the shortened swallowing latency observed across stimulus volumes (Figs. 2 and 3). As well, mechanical sensory testing was performed on the palatal margin and the anterior tonsillar pillars, and although the tip of the infusion catheter was just posterior to those structures, the infusate likely also contacted the posterior pharyngeal wall, where testing cannot be reliably performed because of the gag responses (16). Thus we cannot entirely exclude the possibility that mechanoreceptor function may have been better preserved or potentially increased in a compensatory fashion at the posterior pharyngeal wall. However, the latter seems unlikely, in that although we previously observed varying degrees of sensory impairment at different UA sites in the same patient, we did not identify areas of heightened sensitivity (21).

Another possibility is that the shorter swallowing latency in OSA patients was due to a difference in the rapidity with which the fluid bolus contacts mucosal receptors. Catheter position and fluid bolus infusion rates were the same for both groups. However, UA dimensions are known to be reduced in OSA, and although we did not formally evaluate this, our OSA patients demonstrated typical reductions in oropharyngeal size compared with CL subjects. Thus the fluid bolus may have contacted mucosal receptors more rapidly and, possibly, because of anatomic constraint also produced slightly higher local pressure changes. This might therefore have contributed to the overall reduction in swallowing latency responses in the OSA patients and may also have obscured a relation between sensory threshold levels and swallowing responses in the OSA patients.

Normally, swallowing occurs in expiration and is accompanied by inhibition of the onset of the subsequent inspiration, the functional advantage of which is to minimize the risk of food aspiration (10). In this study, there were minor differences in respiratory-swallowing interactions in OSA patients compared with CL subjects. Although swallowing occurred almost exclusively during expiration in both groups, OSA patients swallowed slightly earlier in the expiratory phase, with the difference in %CCD values between groups achieving statistical significance for swallows that occurred during the same breath as the fluid bolus delivery (Table 3).

Respiratory cycle prolongation after swallowing, measured as IST, was similar for OSA patients and CL subjects (Table 3). However, we observed a significant inverse correlation between the severity of the UA sensory impairment and the duration of postswallowing inspiratory suppression in OSA patients (Fig. 5). This finding suggests that UA mucosal sensory changes influence the central integration of airway function, such that an attenuation of afferent mucosal feedback results in a less potent suppression of inspiratory onset. Thus, as with the reduction in swallowing latency in OSA patients, these results are consistent with a reduction in inhibitory modulating influences on UA motor control.

In conclusion, this study identified mild changes in pharyngeal swallowing responses and respiratory-swallowing interactions in OSA patients, with a loss of inhibitory afferent information, that modulate UA reflex responses and central integration of airway motor control. These changes may therefore have implications for the maintenance of UA patency during sleep in OSA patients. We propose that further investigations are warranted to more extensively evaluate swallowing function in OSA and to determine the relations between UA sensory function assessed during wakefulness and motor control during sleep.

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