



ORIGINAL ARTICLE

Swallowing and aspiration during sleep in patients with obstructive sleep apnea versus control individuals

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Abstract

Study Objectives: There are only a few reports on voluntary swallowing during sleep; therefore, this study aimed to propose a method for observing voluntary swallowing during sleep using polysomnography. The frequency of voluntary swallowing during sleep and the factors related to swallowing and aspiration during sleep were investigated.

Methods: Polysomnography records of 20 control subjects and 60 patients with obstructive sleep apnea (OSA) (mild, moderate, and severe groups; n = 20 each) were collected. Simultaneous increases in the electromyographic potentials of the submental and masseter muscles, termed coactivation, and declining oronasal airflow (SA) were extracted as “swallowing.” The cough reflex that occurred during sleep was extracted as “aspiration.” The frequency of swallowing events was compared among the different OSA severity groups. Subsequently, a multivariate regression analysis was performed.

Results: The average frequency of coactivation with SA in control subjects was 4.1 events/h and that without SA was 1.7 events/h. These frequencies increased with the severity of OSA during non-REM sleep. The distance of the hyoid to the Frankfurt plane was associated with the frequency of coactivation with ($\beta = 0.298$, $p = 0.017$) as well as without SA ($\beta = 0.271$, $p = 0.038$). The frequency of coactivation without SA was associated with aspiration ($B = 0.192$, $p = 0.042$).

Conclusions: Our data provide new insights into the relationship between swallowing and aspiration during sleep. We found that the longer the distance from the hyoid bone to the Frankfurt plane, the higher the coactivation without SA, which could lead to aspiration during sleep.

Clinical Trials: Retrospective observational study of swallowing during sleep in obstructive sleep apnea patients using polysomnography, https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000050460, UMIN000044187.

Statement of Significance

Aspiration pneumonia has garnered substantial clinical attention. Aspiration during sleep is as important as in the awake state; however, there are a few studies on this topic. This is primarily due to the lack of appropriate methods to detect swallowing during sleep. Here, we propose a method for observing voluntary swallowing during sleep and determine the frequency of voluntary swallowing during sleep in subjects without obstructive sleep apnea and in patients with obstructive sleep apnea, as many studies show that patients with obstructive sleep apnea have abnormal swallowing while awake. The association between the frequency of voluntary swallowing and aspiration during sleep was also investigated. Our findings may improve understanding of the physiological and pathological roles of aspiration during sleep.

Key words: deglutition; hyoid bone; obstructive sleep apnea; polysomnography; respiratory aspiration; sleep

Submitted: 20 October, 2021; Revised: 7 January, 2022

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Introduction

Swallowing and breathing share a passage in the pharynx. During swallowing, the oral, pharyngeal, esophageal, and respiratory systems act in concert and protect the airway from aspiration [1–3]. Therefore, dysfunctions of these systems may lead to aspiration [4]. Swallowing and aspiration occur during sleep, as in the awake state; however, there are a few reports on these events during sleep, and the cause of aspiration remains unknown [5–8].

The swallowing process can be divided into consecutive oral, pharyngeal, and esophageal phases [9]. In the oral phase (voluntary phase), the mouth is closed, the tongue is elevated, and the oral cavity is temporarily sealed. The pharyngeal phase (involuntary phase) starts with the stimulation of the neural afferents in the oropharynx [10, 11]. When the swallowing reflex starts, the larynx is pulled up so that the epiglottis covers the entrance to the trachea. During swallowing, swallowing apnea occurs, which is an involuntary pause in ventilation that normally lasts for 0.5–1.0 s [12–15]. The healthy swallowing reflex is well-coordinated with the respiratory pattern [1, 11, 16–20], and changes in respiratory patterns impair the coordination of swallowing and breathing [21, 22].

There are also many reports on swallowing in patients with sleep apnea [23–42]. One study compared swallowing reflexes between control subjects and patients with sleep apnea by inducing swallowing with water while awake. The results revealed that the time between water bolus injection and the onset of swallowing was increased in patients with sleep apnea, causing an abnormal swallowing reflex [42]. A recent study by Pizzorni et al. [36] reported that 15% of patients with OSA ($N = 951$) had symptoms of dysphagia, and 35 of these underwent a fiberoptic endoscopic evaluation of swallowing. Furthermore, patients with OSA had a lower bolus location at swallow onset, greater pharyngeal residue, and higher frequency and severity of penetration and aspiration events when compared to healthy subjects. However, they were unable to identify any associations between polysomnographic indices and dysphagia symptoms in patients with OSA using standard polysomnographic indices routinely used in clinical practice; therefore, they recommended the use of other polysomnographic indices in future studies to identify associations. In addition, a large epidemiological study of 34,100 people reported that patients with sleep apnea were at a 1.2-fold higher risk of pneumonia [43].

By observing voluntary swallowing of patients with sleep apnea during sleep, the effect of abnormal swallowing reflexes on swallowing during sleep can be investigated. A better understanding of the relationship between abnormal swallowing reflex and aspiration during sleep may help elucidate the mechanism of aspiration during sleep, as well as improve sleep apnea management.

Regarding the noninvasive observation method of swallowing, swallowing-associated maxillofacial muscle activity has been recorded using surface electromyograms during the awake state [11, 44–51]. According to these studies, when swallowing was induced in the participants, surface electromyogram (EMG) activities of the masseter, temporalis, pterygoid, and submental muscles occurred during the oral phase of swallowing. The masseter, temporalis, and pterygoid muscles are used to close the mouth. The submental muscle is used for elevating the tongue. Furthermore, some researchers have also examined swallowing

apnea by recording changes in respiration during the awake state [16, 17, 52–54].

In this study, we proposed a method for observing voluntary swallowing during sleep, using polysomnography. Simultaneous activity of the masseter muscle EMG and submental muscle EMG (coactivation), as well as swallowing apnea (SA), were monitored. The frequency of voluntary swallowing during sleep was determined, and the factors related to swallowing and aspiration during sleep were investigated.

Methods

This retrospective observational study was approved by the ethical review committee of Nippon Dental University at Niigata (ECNG-R-429) and was registered in the UMIN Clinical Trial Registry (UMIN000044187, May 12, 2021; https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000050460). Only data from patients who agreed to the use of the data obtained from examinations and treatments as research material were included. In addition, information on the research was made available on the university website, and the data were collected after confirming that there was no withdrawal of consent.

Subjects

Polysomnography and cephalography data of patients who visited the Dental Sleep Medicine Center at Nippon Dental University Niigata Hospital certified by the Japanese Society of Sleep Research and underwent polysomnography for detailed examination of obstructive sleep apnea (OSA) were included. The exclusion criteria were as follows: refusal to participate in this study or the presence of deglutition disorders, neurological disorders, respiratory disorders, maxillofacial deformities requiring surgical treatment, odontoparallaxis, and malocclusion.

A total of 95 consecutive subjects were enrolled in the study and 15 were excluded (No consent: 10, Insufficient recorded data: 3, Neurological disorders: 2); therefore, 80 subjects ($n = 43$ males, $n = 37$ females) were included in the final analysis. The average age was 53.9 ± 15.4 years.

Polysomnography records

Polysomnography was performed using a polysomnography system (SAS1100, NIHON KOHDEN, Inc., Tokyo, Japan) in a quiet room in the hospital. The monitoring items were as follows: electroencephalogram (EEG), bilateral electrooculogram (EOG), submental muscle-EMG and masseter muscle-EMG, snoring sounds, airflow (using a nasal pressure cannula and oronasal thermistor), inductive bands on the chest and abdomen, electrocardiogram (ECG), percutaneous oxygen saturation, surface EMG of the bilateral anterior tibialis muscles, body position, and video recording with a night-vision camera.

Silver–silver chloride electrodes with a diameter of 8 mm (NIHON KOHDEN, Inc.) were used for EEG, EOG, EMG, and ECG recordings and arranged according to the American Academy of Sleep Medicine (AASM) scoring manual [55]. Two bipolar surface electrodes on the left and right were used for masseter muscle-EMG; these were placed on the muscle belly of the masseter muscle along a muscle fiber and exocanthion–gonion line, with the upper electrode placed under the tragus labial commissural

line [45]. After all the sensors were placed, calibration was performed, including for spontaneous swallowing, mouth opening, and closing.

Sleep stages and respiratory events were analyzed by professional clinical laboratory technologists certified by the Japanese Society of Sleep Research. Scoring of sleep stages and respiratory events was performed based on the AASM scoring manual [55], whereby criteria for hypopnea were defined as a decrease of 30% or more in nasal pressure and 4% or more in oxygen desaturation.

Based on the apnea-hypopnea index (AHI) analyzed, polysomnography records were grouped according to OSA severity. Patients whose AHI was less than 5 events/h were allocated to the control group, those with 5 to less than 15 events/h were allocated to the mild group, those with 15 to less than 30 events/h were allocated to the moderate group, and those with more than 30 events/h were allocated to the severe group. Control subjects were referring to patients who visited our center with complaints of sleepiness or snoring whose PSG test results showed no pathological sleep disorder.

Detection of swallowing movements from polysomnography records

Polysomnography records were visually analyzed to identify swallowing movements by an investigator blinded to patient information. All simultaneous increases in the excitation of waveform potentials of submental muscle-EMG and masseter muscle-EMG during sleep, termed coactivation, were extracted. Airflow waveforms before and after each coactivation were similarly assessed. SA was evaluated mainly using an oronasal airflow (thermistor) with good sensitivity. Since the change in respiratory waveform differs depending on the respiratory phase during swallowing, a sample of the change in the respiratory waveform for each respiratory phase during swallowing was created with reference to the report by Paydarfar et al. [1]. Subsequently, the corresponding respiratory waveform was determined to be SA. Three oronasal airflow waveforms before coactivation were used as the typical respiratory waveforms before swallowing.

To extract only the coactivation frequency during sleep, only the polysomnography epochs (judged by professional clinical laboratory technologists with 20 years of experience) related to the sleep state were targeted, and those related to arousal and the awake state were excluded from the analysis.

Detection of aspiration during sleep

The night-vision camera recording was used with the polysomnography waveform to extract the cough reflex that occurred during sleep, which was considered to reflect aspiration.

Cephalometric radiograph analysis

Cephalometric radiographs (Figure 1) were obtained for diagnosis under the following conditions: awake, upright, resting expiratory level during nasal breathing, and maximal intercuspal position, before the polysomnography test. To assess the skeletal structure, cephalometric radiographs were reanalyzed by an investigator (A.K.) blinded to patient information, using

a cephalometric analysis program (WinCeph version 10, Rise Corporation, Miyagi, Japan). The analysis items were the angle between the S-N and the N-A line (SNA) and the angle between the S-N and N-B line (SNB), which indicate the anteroposterior position of the maxilla and the mandible with respect to the cranial base, respectively. Additionally, we analyzed the angle between the Ba-N and Pt-(Intersection of N-Pog[R] and Go[L]-Me) lines (facial axis angle of Ricketts), which indicates the direction of mandibular growth with respect to the cranial base. The distance of the hyoid to the Frankfurt plane (FPH) was also measured [56].

Statistical analysis

The primary outcomes were the frequency of voluntary swallowing and aspiration during sleep, which were compared between control subjects and patients with OSA. The secondary outcomes were factors related to the frequency of voluntary swallowing and aspiration during sleep. Values are presented as means (standard deviation) and median (first quartile-third quartile).

The sample size was calculated using Gpower 3.1 [57, 58] with $f = 0.4$, $\alpha = 0.05$ (two-sided), and $1 - \beta = 0.8$. The minimum total sample size was calculated as 76. The polysomnography records were collected from consecutive patients from the control group and from each OSA severity group (mild, moderate, and severe) since January 15, 2021.

Age, sex, body mass index (BMI), SNA, SNB, facial axis, FPH, sleep efficiency, the appearance rate of non-REM sleep, and REM sleep were compared between control subjects and patients with OSA. A normality test (Shapiro-Wilk test) was performed for items other than sex. Unpaired t-tests were applied if the data had a normal distribution, while Mann-Whitney's U test



Figure 1. Cephalometric analysis. Cephalograms were obtained under the standing, occlusal, and resting expiratory conditions. A, subspinale; B, supramentale; Ba, basion; Facial axis angle of Ricketts, angle between Ba-N and Pt-(Intersection of N-Pog[R] and Go[L]-Me) line; FPH, distance of the hyoid to the Frankfurt plane (Or-Po line); Go[L], lower gonion; Me, menton; N, nasion; Or, orbitale; Po, porion; Pog[R], pogonion (Ricketts); Pt, pterygomaxillary fissure; S, sella; SNA, angle between SN and NA line; SNB, angle between SN and NB line.

was applied if the data were not normally distributed. For sex comparisons, a chi-square test was performed.

The frequency of swallowing movements was calculated by dividing the number of swallowing movements by total sleep time. The frequency of aspiration per night was counted and compared between control subjects and patients with OSA. In addition, the frequency of swallowing movements of non-REM sleep or REM sleep was also calculated by dividing the number of swallowing movements of each sleep stage by the total duration of each sleep stage. The frequency of aspiration during non-REM sleep and during REM sleep were counted. The statistical method for comparing control subjects and patients with OSA was also as described above. Moreover, a comparison between non-REM sleep and REM sleep was performed. A normality test (Shapiro-Wilk test) was performed, and the paired t-test was used if the data distribution was homoscedastic, while the Wilcoxon signed-rank test was used if the data distribution did not follow such a distribution.

In the comparison among the four groups according to OSA severity, a normality test (Shapiro-Wilk test) was performed, and one-way analysis of variance (ANOVA) and the Tukey test were applied if the items were normally distributed and homoscedastic, while One-way ANOVA with Welch test and the Games-Howell test were applied if the items had a healthy but not homoscedastic distribution, and the Kruskal-Wallis test was applied to variables with distributions other than the healthy distribution.

For secondary outcomes, multiple linear regression analysis was performed using the forced input method, with the dependent variable being the frequency of swallowing movements and the independent variable being the item associated with the severity of OSA. In addition, binomial logistic regression analysis was performed using the variable reduction method based on the likelihood ratio, with the item indicating the presence or absence of aspiration as the dependent variable and age, sex, BMI, SNA, SNB, facial axis, FPH, sleep efficiency, and the frequency of swallowing movement as the independent variables. A correlation matrix was created in advance when inputting the independent variables to confirm that there was no coarse correlation with $r > 0.80$ among the independent variables.

IBM SPSS Statistics version 25 (IBM, Armonk, NY, USA) was used for all statistical analyses. Statistical significance was set at $p < 0.05$.

Results

Table 1 shows the comparison between control subjects and patients with OSA based on patient characteristics, the results of cephalometric radiograph analysis, and the polysomnography test. The unpaired t-test was applied to comparisons of age, BMI, SNA, SNB, facial axis, FPH, and sleep stage rate, and the Mann-Whitney U test was applied to comparisons of sleep efficiency. Significant differences between control subjects and patients with OSA were observed in age ($p = 0.030$), BMI ($p = 0.015$), and FPH ($p < 0.001$). The OSA group was older and had a higher BMI and a longer pharyngeal length than the control group.

Table 2 shows the frequencies of swallowing movements and aspiration during sleep. Two types of swallowing events were observed during sleep: coactivation with SA and coactivation without SA (Figure 2). The unpaired t-test was applied to overall coactivation, overall coactivation during non-REM sleep,

coactivation with SA, and coactivation with SA during non-REM sleep. Mann-Whitney's U test was applied to all other comparisons. The Wilcoxon signed-rank test was used to compare non-REM sleep and REM sleep. Swallowing movement in non-REM sleep was significantly higher in the OSA group than in the control group (overall coactivation, $p < 0.001$; coactivation with SA, $p < 0.001$; coactivation without SA, $p < 0.001$), whereas there was no significant difference between the groups in REM sleep.

Table 3 shows the comparison of the frequency of swallowing events among the groups according to OSA severity. One-way ANOVA and Tukey's test were applied to coactivation with SA, and One-way ANOVA with Welch test and the Games-Howell test was applied to overall coactivation and coactivation with SA during non-REM sleep. The Kruskal-Wallis test was applied to other comparisons. The frequency of swallowing movement during non-REM sleep increased with the severity of OSA (overall coactivation, $p = 0.001$; coactivation with SA, $p = 0.003$; coactivation without SA, $p = 0.005$), but the percentage of coactivation without SA was constant with no difference.

Table 4 shows the factors related to the frequency of swallowing events. The items related to AHI in Table 1 (age, BMI, FPH, and sleep efficiency) were examined. FPH was most strongly associated with the frequency of swallowing events (overall coactivation: $\beta = 0.345$, $p = 0.006$, coactivation with SA: $\beta = 0.298$, $p = 0.017$, coactivation without SA: $\beta = 0.271$, $p = 0.038$), indicating that the further the caudal displacement of the hyoid, the higher is the frequency of swallowing events.

Table 5 presents the factors related to aspiration during sleep. Sleep efficiency and the frequency of coactivation without SA were selected by stepwise selection. An increased frequency of coactivation without SA was a risk factor for aspiration during sleep ($B = 0.192$, $p = 0.042$, odds ratio = 1.212).

Discussion

Voluntary swallowing during sleep

Coactivation with SA and coactivation without SA were observed during sleep. Since SA indicates the presence of the swallowing reflex, coactivation with SA is considered to be a swallowing movement that triggers the swallowing reflex, while coactivation without SA is considered to be a swallowing movement that does not trigger the swallowing reflex. Therefore, coactivation with SA was termed as complete swallowing, and coactivation without SA was termed as incomplete swallowing.

There have been several studies that have observed swallowing during sleep, and they found that laryngeal movements are associated with the swallowing reflex. In particular, they reported swallowing frequencies of 5.3 ± 1.7 , 5.8 , and 2.9 ± 1.3 events/h while sleeping in 20, 10, and 8 subjects, respectively [5, 6, 59]. These values are considered to correspond to the frequency of complete swallowing in this study, and the frequency noted in our study was 4.1 ± 2.2 events/h in control subjects, which was consistent with same values reported in the previous reports on laryngeal movements. Although laryngeal movement is an efficient indicator to observe swallowing, stable recording of laryngeal movement may be difficult, especially in severely ill patients with OSA because they may be obese and have a lot of fat near the larynx or frequent laryngeal movements due to breathing efforts. Therefore, we selected the masseter and submental muscles, which are less affected by extra fat around the muscles.

Table 1. Patient characteristics and results of cephalometric radiograph analysis and polysomnography in control subjects and patients with obstructive sleep apnea

	All	Control	OSA	P value
Age (years)	53.9 (15.4)	47.5 (16.4)	56.1(14.6)	0.030
	54.0 (44.0–65.3)	45.0 (31.8–55.8)	55.0 (49.0–67.3)	
Sex (male:female)	43:37	7:13	36:24	n. s
BMI (kg/m ²)	24.9 (5.0)	22.6 (3.2)	25.7(5.2)	0.015
	24.2 (21.3–26.9)	22.1 (20.4–24.2)	25.3 (22.6–27.1)	
SNA (°)	83.7 (3.4)	83.1 (2.4)	83.9 (3.6)	n. s
	83.5 (81.7–85.4)	83.2 (82.2–83.8)	83.6 (81.7–85.5)	
SNB (°)	79.1 (4.0)	78.9 (3.8)	79.2 (4.1)	n. s
	79.0 (77.0–81.2)	78.2 (76.8–81.4)	79.0 (77.1–80.9)	
Facial axis (°)	85.2 (4.8)	85.6 (4.8)	85.0 (4.8)	n. s
	85.5 (82.0–88.2)	86.1 (83.7–89.1)	85.3 (81.8–88.0)	
FPH (mm)	103.6 (9.9)	97.2 (6.7)	105.7(10.1)	<0.001
	103.2 (97.8–109.8)	98.7 (90.4–101.7)	105.9 (100.0–111.0)	
Sleep efficiency (%)	76.9 (14.8)	76.4 (19.1)	77.1(13.3)	n. s
	82.0 (67.9–86.4)	85.5 (64.5–89.7)	81.4 (68.3–85.8)	
Non-REM sleep (%)	85.5 (5.1)	85.8 (5.8)	85.5 (5.0)	n. s
	85.4 (82.4–88.1)	85.5 (82.1–88.0)	85.2 (82.5–88.4)	
REM sleep (%)	14.5 (5.1)	14.2 (5.8)	14.5 (5.0)	n. s
	14.7 (11.9–17.5)	14.6 (12.1–17.9)	14.9 (11.7–17.5)	
AHI (events/h)	20.7 (19.4)	2.1 (1.4)	26.9 (18.6)	–
	14.7 (5.2–30.1)	1.7 (1.1–3.1)	20.9 (10.9–41.8)	

Abbreviations: AHI, apnea hypopnea index; BMI, body mass index; Facial axis, angle between Ba-N and Pt-(Intersection of N-Pog[R] and Go[L]-Me) line; FPH, the distance of the hyoid to the Frankfurt plane; OSA, obstructive sleep apnea; REM or non-REM sleep, the appearance rate of the respective sleep stages; SNA, angle between S-N and N-A line; SNB, angle between S-N and N-B line.

In the table, the values given above are means (standard deviation), and those given below are median (first quartile–third quartile). The unpaired t-test was applied to comparisons of age, BMI, SNA, SNB, facial axis, FPH, and sleep stage rate; and the Mann-Whitney U test was applied to comparisons of sleep efficiency. *p* value relates to the comparison between control and obstructive sleep apnea groups overall.

In this study, we showed that, even in control subjects, incomplete swallowing occurs, and when coactivation occurs during sleep, complete swallowing and incomplete swallowing occur at a certain rate. Therefore, patients with OSA may have increased frequencies in both complete and incomplete swallowing due to increased coactivation.

The reason for this increase in coactivation may be an increase in incomplete swallowing, related to the caudal position of the hyoid bone. Studies of induced swallowing during arousal have reported that patients with OSA have a delayed swallowing onset [42]. Caudal displacement of the hyoid bone is one of the features of patients with OSA. This displacement of the hyoid bone may make it difficult to lift the larynx to the position required for swallowing, causing a delay in swallowing onset. In addition, it has been reported that prolonged intervals to laryngeal vestibule closure may lead to unsafe deglutition and aspiration in older patients with neurogenic dysphagia and aspiration associated with stroke [60]. Since aspiration was observed in subjects with more incomplete swallowing, it was considered that a delay in the onset of swallowing may lead to incomplete swallowing. With incomplete swallowing, the pharynx is not cleared, and the substances accumulated without swallowing may then stimulate swallowing and induce coactivation (Figure 3). Although only incomplete swallowing was expected to increase, results revealed increased frequencies in both complete and incomplete swallowing due to increased coactivation in patients with OSA.

Swallowing during sleep in patients with OSA

This is the first study to investigate the relationship between pharyngeal length and swallowing. We unexpectedly found that

the pharyngeal length was more strongly associated with the frequency of swallowing during sleep than with AHI.

Many studies on swallowing in patients with OSA have reported that patients with OSA have impaired sensory and motor function of the pharyngeal structure, due to the low-frequency vibrations of habitual snoring and presence of abnormal signs of swallowing [23–37, 39–42]. These factors are thought to be involved in the delay of the onset of swallowing [42]. In this study, we predicted that the frequency of apnea and hypopnea events would be strongly associated with the frequency of incomplete swallowing. The more apnea and hypopnea events, the more laryngeal movement occurred due to breathing effort, and the more unstable was the switching between breathing and swallowing. We considered this to be related to swallowing and aspiration during sleep. However, our results were different. Since many patients with OSA have a longer pharynx, it is possible that previous studies had related AHI to the frequency of swallowing during sleep [61].

Differences in swallowing during non-REM sleep and REM sleep

As there was no difference in the frequency of swallowing during REM sleep between the control and OSA groups, it seemed possible that the incidence of REM sleep per se was low and that it was insufficient to compare the frequency of swallowing during REM sleep. However, another possibility was that changes in respiratory muscle function during the transition from non-REM sleep to REM sleep played a role [62–66].

The hyoid bone moves caudally due to increased lung volume during inspiration, possibly as a means to prevent the airway from collapsing [56]. During REM sleep,

Table 2. The frequency of swallowing movement and aspiration during sleep

Swallowing events	Sleep stage	Control	OSA	P value
Overall coactivation (events/h)	Total	6.0 (2.6) 6.6 (3.5–7.4)	10.4 (5.7) 9.2 (6.4–14.5)	<0.001
	Non-REM	5.7 (2.7) 5.7 (3.5–7.2)	11.0 (6.1) 10.4 (6.6–15.4)	<0.001
	REM	8.1 (7.2) 4.9 (2.9–11.9)	9.4 (13.5) ** 5.2 (3.1–10.7)	n. s
Coactivation with swallowing apnea (events/h)	Total	4.1 (2.2) 4.6 (2.4–5.3)	6.6 (3.8) 6.0 (4.2–8.5)	0.007
	Non-REM	4.1 (2.2) 3.9 (2.5–5.7)	7.0 (4.2) 6.4 (4.4–9.3)	<0.001
	REM	5.6 (5.4) 3.5 (1.8–9.6)	6.4 (11.7) ** 3.3 (1.4–7.1)	n. s
Coactivation without swallowing apnea (events/h)	Total	1.7(1.0) 1.6 (1.0–2.1)	3.8 (3.0) 2.8 (1.8–5.7)	0.002
	Non-REM	1.6 (0.9) 1.4 (0.9–2.1)	4.0 (3.2) 2.9 (1.6–5.8)	<0.001
	REM	2.3 (2.8) 1.8 (0.0–3.5)	3.0 (3.8) ** 1.7 (0.0–4.2)	n. s
Percentage of coactivation without swallowing apnea (%)	Total	28.6 (11.9) 24.4 (20.2–38.9)	35.8 (15.3) 35.1 (27.7–44.4)	0.025
	non-REM	28.7 (12.2) 26.1 (19.9–38.5)	35.6 (15.7) 0.4 (0.2–0.4)	n. s
	REM	31.3 (27.9) 31.0 (2.4–48.9)	35.2 (32.7) 0.3 (0.0–0.6)	n. s
Aspiration (events/night)	Total	1.7 (2.0) 1.0 (0.0–2.3)	1.6 (2.7) 0.0 (0.0–2.0)	n. s
	non-REM	1.4 (2.1) 0.5 (0.0–2.0)	1.3 (2.5) 0.0 (0.0–1.3)	n. s
	REM	0.3 (0.6) * 0.0 (0.0–0.3)	0.3 (0.7) ** 0.0 (0.0–0.0)	n. s

Total frequency of swallowing events and the comparison of the frequency between control and obstructive sleep apnea (OSA) groups, and between nonrapid eye movement (REM) sleep and REM sleep. Percentage of coactivation without swallowing apnea (SA): the ratio of coactivation without SA to overall coactivation. Values given above are the means (standard deviation), and those given below are the median (first quartile–third quartile). The unpaired t-test was applied to coactivation, coactivation during non-REM sleep, coactivation with SA, and coactivation with SA during non-REM sleep. Mann–Whitney’s U test was applied to all other comparisons. The Wilcoxon signed-rank test was used to compare non-REM sleep and REM sleep. The P value represents the comparison between control and OSA groups.

*: $p < 0.05$

†: $p < 0.01$ vs. non-REM sleep.

diaphragm-dominant breathing occurs and lung volume decreases [62–65], and the hyoid bone accordingly moves to the cranial side. It is possible that the shortening of the pharynx eliminated the difference in the frequency of swallowing between the control and OSA groups during REM sleep. As a result, there was no difference in the frequency of swallowing between non-REM sleep and REM sleep in control subjects, whereas the frequency of swallowing decreased in REM sleep in patients with OSA.

Aspiration during sleep

Some aspirations does not cause cough reflex; however, there is no method to assess aspiration that does not trigger the cough reflex [67]. Silent aspiration is considered to be related to the laryngeal cleft, laryngomalacia, unilateral vocal fold paralysis, developmental delay, epilepsy/seizures, congenital heart disease, brain cancer, brain stroke, head–neck cancer, pneumonia, dementia/Alzheimer’s disease, chronic obstructive lung disease, myocardial infarcts, and neurodegenerative conditions [68, 69]. As this study did not include patients with these disorders, the frequency of the cough reflex during sleep determined in our study was meaningful.

Premature oral leakage to the pharynx, pharyngeal stasis, and laryngeal penetration were considered to be the cause of aspiration during sleep [70]. The frequency of incomplete swallowing may reflect the presence of these phenomena. Examining the frequency of incomplete swallowing during sleep may be useful in determining the risk of aspiration and silent aspiration during sleep.

Clinical implications of the study

It was suggested that improving the caudal displacement of the hyoid bone may prevent incomplete swallowing and aspiration during sleep. Oral appliances used to treat OSA may also improve swallowing during sleep because they displace the hyoid bone to the cranial side [71, 72]. Furthermore, the position of the hyoid bone changes depending on the flexion and extension of the neck [73]. Extension of the neck is an effective approach to airway management [74]. It is considered that a flexed position of the neck is effective for swallowing during sleep. Therefore, to prevent aspiration during sleep, it may be important to sleep in a posture in which the neck is flexed while securing the airway with continuous positive airway pressure or oral appliances as necessary.

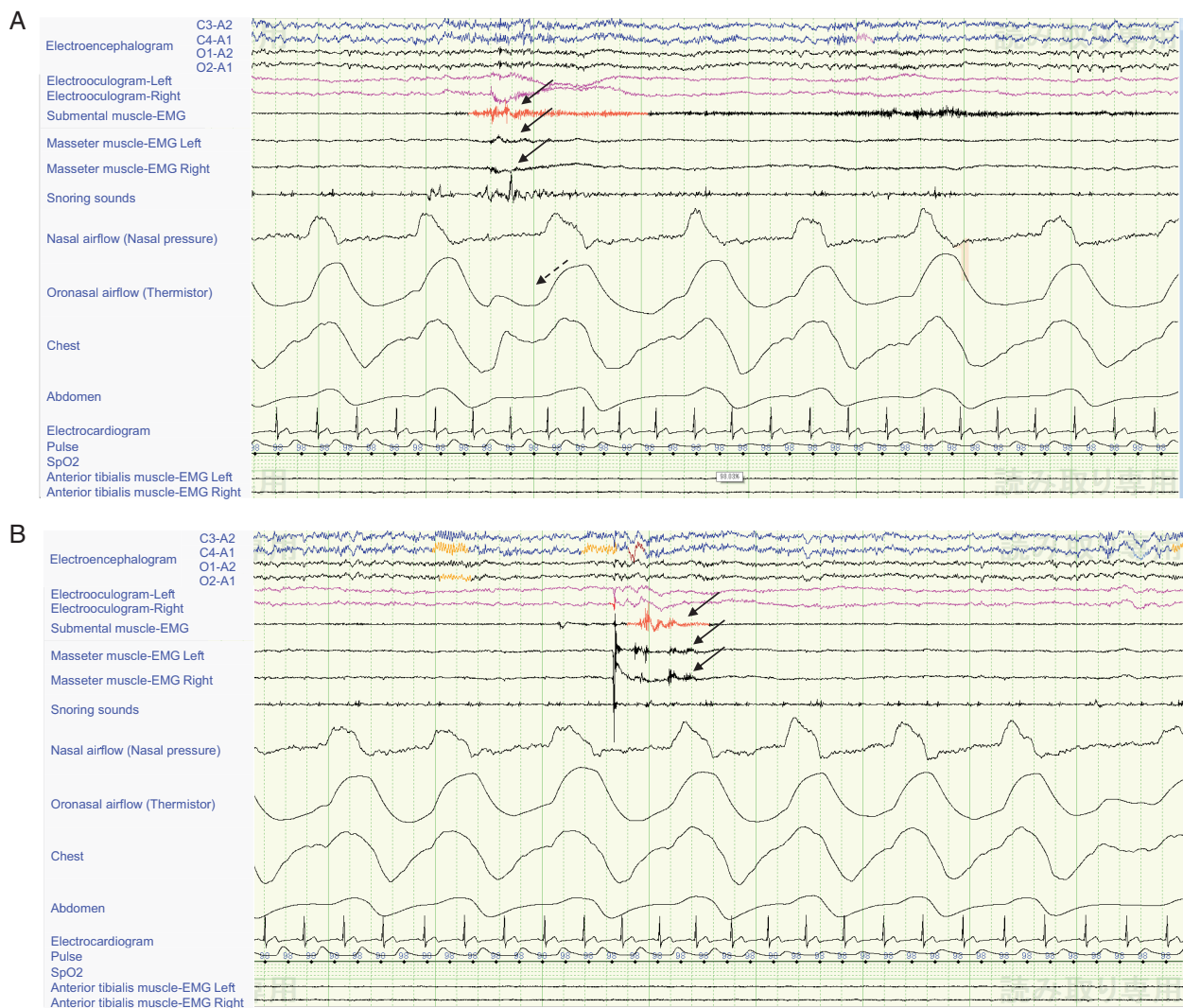


Figure 2. Detection of swallowing. (a) Coactivation with swallowing apnea, and (b) coactivation without swallowing apnea. A simultaneous increase in the excitation of waveform potentials of submental muscle-electromyogram (EMG) and masseter muscle-EMG (L and R), termed coactivation (solid-line arrows), was identified. It was accompanied by a decline in oronasal airflow (dotted-line arrow) (a). Coactivation (solid-line arrows) was identified, but there was no change in respiratory waveform before and after coactivation (b).

The cause of caudal displacement of the hyoid bone is considered to be infra-hyoid muscle activation [75, 76], displacement of excessive soft tissue [77, 78], and tracheal traction by lung inflation [73, 79]. These phenomena are common in patients with OSA. Therefore, early initiation of OSA treatment prevents caudal displacement of the hyoid bone and may prevent incomplete swallowing and aspiration during sleep. In addition, without considering the position of the hyoid bone, it may be possible to control the increase or decrease in incomplete swallowing by changing the swallowing threshold.

Limitations

This study was conducted on a small cohort of a limited demographic group in a single medical center. Large-scale surveys in different facilities are necessary to confirm our results. Similar studies can be performed by simply adding swallowing analysis to the normal polysomnography analysis.

Furthermore, future studies should investigate the relationship between incomplete swallowing and aspiration that does

not cause the cough reflex. This will require the development of a method to extract this particular process.

Conclusion

Our data provided insight into the relationship between swallowing and aspiration during sleep. These findings contribute to the understanding of the physiological and pathological role of aspiration during sleep. The results showed that incomplete swallowing can be reduced by moving the hyoid bone to the cranial side and shortening the distance of the hyoid to the Frankfurt plane. This procedure may prevent aspiration during sleep.

Acknowledgments

We would like to thank the staff of the Dental Sleep Medicine Center at Nippon Dental University Niigata Hospital, certified by the Japanese Society of Sleep Research.

Table 3. Comparison of the frequency of swallowing events among groups by obstructive sleep apnea severity

Swallowing events	Sleep stage	Severity of obstructive sleep apnea				P value
		Normal	Mild	Moderate	Severe	
Overall coactivation (events/h)	Total	6.0 (2.6)	10.1 (6.9)	10.1 (5.2) *	10.9 (5.1) **	<0.001
	non-REM	6.6 (3.5–7.4)	9.2 (4.9–14.3)	9.2 (6.9–11.6)	10.5 (6.4–14.6)	0.001
		5.7 (2.7)	10.3 (7.3)	11.0 (5.9) **	11.8 (5.3) **	
	REM	5.7 (3.5–7.2)	9.9 (4.2–14.8)	9.9 (7.3–13.2)	12.6 (7.1–15.7)	n. s
4.9 (2.9–11.9)	6.8 (4.4–11.6)	5.0 (3.1–9.5)	3.7 (2.2–10.9)			
Coactivation with swallowing apnea (events/h)	Total	4.1 (2.2)	6.0 (3.9)	6.3 (3.4)	7.3 (4.2) *	0.034
	non-REM	4.6 (2.4–5.3)	5.8 (3.2–8.6)	5.8 (4.5–7.8)	6.4 (4.2–9.9)	0.003
		4.1 (2.2)	6.3 (4.3)	7.0 (4.0) *	7.9 (4.5) *	
	REM	3.9 (2.5–5.7)	6.2 (2.8–8.5)	5.8 (4.5–8.3)	6.7 (4.4–11.3)	n. s
3.5 (1.8–9.6)	4.5 (2.5–7.9)	2.8 (1.8–5.4)	2.6 (0.8–8.1)			
Coactivation without swallowing apnea (events/h)	Total	1.7 (1.0)	4.1 (3.6)	3.8 (2.9) *	3.6 (2.6)	0.018
	non-REM	1.6 (1.0–2.1)	2.4 (1.2–6.2)	3.5 (1.9–4.8)	2.8 (2.2–5.0)	0.005
		1.6 (0.9)	4.0 (3.8)	4.0 (3.3) *	3.9 (2.8) **	
	REM	1.4 (0.9–2.1)	2.4 (1.4–6.4)	3.6 (1.8–5.5)	3.1 (2.5–5.4)	n. s
2.3 (2.8)	4.3 (4.6)	2.7 (3.3)	2.0 (3.0)			
Percentage of coactivation without swallowing apnea (%)	Total	1.8 (0.0–3.5)	3.0 (0.9–5.5)	1.6 (0.0–3.4)	0.0 (0.0–3.0)	n. s
	non-REM	28.6 (11.9)	38.1 (13.5)	35.6 (15.8)	33.7 (17.0)	n. s
		24.4 (20.2–38.9)	36.8 (28.8–45.4)	35.0 (28.8–41.5)	33.1 (20.8–46.0)	
	REM	28.7 (12.2)	37.4 (16.6)	34.9 (14.0)	34.5 (17.0)	n. s
26.1 (19.9–38.5)	36.5 (26.1–42.2)	35.6 (28.5–40.7)	33.8 (21.4–47.9)			
Aspiration (events/night)	Total	31.3 (27.9)	43.8 (32.8)	32.6 (30.2)	27.9 (34.7)	n. s
	non-REM	31.0 (2.4–48.9)	47.7 (14.6–64.9)	30.0 (2.5–50.0)	11.1 (0.0–50.0)	0.006
		1.7 (2.0)	2.2 (3.6)	0.3 (0.7)	2.4 (2.6)††	
	REM	1.0 (0.0–2.3)	0.5 (0.0–3.0)	0.0 (0.0–0.0)	1.5 (0.8–2.5)	n. s
1.4 (2.1)	2.0 (3.5)	0.3 (0.7)	1.7 (2.3)			
0.5 (0.0–2.0)	0.0 (0.0–3.0)	0.0 (0.0–0.0)	1.0 (0.0–2.0)			
0.3 (0.6)	0.2 (0.4)	0.0 (0.0)	0.6 (1.0)††	0.013		
0.0 (0.0–0.3)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–1.0)			

REM, rapid eye movement; Percentage of coactivation without swallowing apnea: the ratio of coactivation without SA to overall coactivation. The values in the table indicate the mean (standard deviation), and those given below are the median (first quartile–third quartile). One-way ANOVA and Tukey's test was applied to coactivation with SA. One-way ANOVA with Welch test and Games–Howell test was applied to overall coactivation and coactivation with SA during non-REM sleep. The Kruskal–Wallis test was applied to all other comparisons. The P value represents the comparison among the four groups defined by obstructive sleep apnea severity.

*: $p < 0.05$

†: $p < 0.01$ vs. Normal

††: $p < 0.01$ vs Moderate.

Table 4. Factors related to the frequency of swallowing movement during sleep

Dependent variable	Independent variable	Standardized regression coefficient	P value	95% confidence interval		Variance inflation factor
				Lower limit	Upper limit	
Overall coactivation (events/h)	FPH (mm)	0.345	0.006	0.055	0.324	1.362
	AHI (events/h)	0.139	0.349	–0.043	0.122	1.970
	Age (years)	–0.092	0.446	–0.117	0.052	1.297
	BMI (kg/m ²)	–0.071	0.563	–0.346	0.190	1.370
Coactivation with swallowing apnea (events/h)	Constant	0.398	0.017	–24.992	10.034	
	FPH (mm)	0.298	0.017	0.020	0.200	1.362
	AHI (events/hour)	0.212	0.155	–0.015	0.095	1.970
	BMI (kg/m ²)	–0.142	0.253	–0.283	0.075	1.370
Coactivation without swallowing apnea (events/h)	Age (years)	–0.067	0.575	–0.072	0.040	1.297
	Constant	0.632	0.038	–14.530	8.883	
	FPH (mm)	0.271	0.038	0.004	0.149	1.362
	Age (years)	–0.114	0.364	–0.066	0.025	1.297
Aspiration (events/night)	AHI (events/h)	0.040	0.798	–0.039	0.050	1.970
	BMI (kg/m ²)	0.014	0.912	–0.136	0.152	1.370
	Constant	0.418	0.017	–13.259	5.567	

The table shows the results of multiple linear regression analysis based on the forced input method. BMI, body mass index; FPH, The distance of the hyoid to the Frankfurt plane; AHI, apnea/hypopnea index. There were no outliers with predicted values exceeding ± 3 standard deviations with respect to the measured values.

Table 5. Factors related to aspiration during sleep

	Regression coefficient	Standard error	P value	Odds ratio	95% confidence interval	
					Lower limit	Upper limit
Coactivation without swallowing apnea (events/h)	0.192	0.094	0.042	1.212	1.007	1.458
Sleep efficiency (%)	-0.030	0.017	0.067	0.970	0.939	1.002
Constant	1.824	1.290	0.157	6.197		

The table shows the results of binomial logistic regression analysis based on the step-down procedure using the likelihood ratio. The *p* value of the omnibus test was 0.024 and that of the Hosmer and Lemeshow test was 0.055.

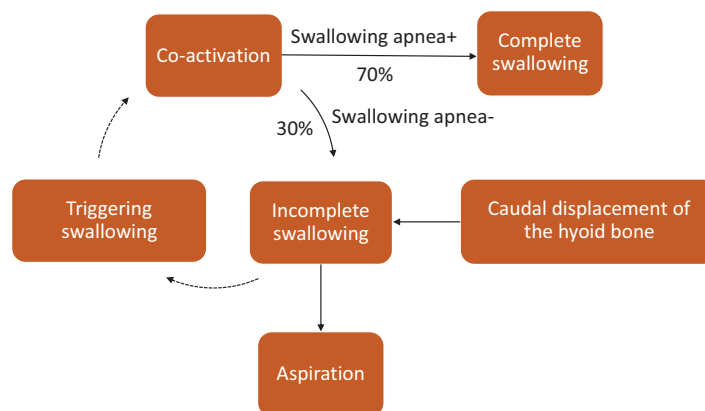


Figure 3. Diagram of the relationship of swallowing with aspiration during sleep. Even in control subjects, when coactivation occurs, approximately 70% of occurrences will involve complete swallowing, and about 30% will involve incomplete swallowing. Caudal displacement of the hyoid bone increases the frequency of incomplete swallowing. Incomplete swallowing cannot clear the pharynx; therefore, substances that are not swallowed accumulate in the pharynx, triggering swallowing and causing coactivation. Aspiration then occurs during incomplete swallowing.

Disclosure Statements

Financial Disclosure: none

Non-financial Disclosure: none

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author and pending approval from Nippon Dental University Niigata Hospital.

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