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ORIGINAL ARTICLE

Pharyngeal Swallowing During Wake and Sleep

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Abstract

Sleep is associated with stages of relative cortical quiescence, enabling evaluation of swallowing under periods of reduced consciousness and, hence, absent volition. The aim of this study was to measure and characterize changes in the characteristics of pharyngeal swallows during sleep and wake using high-resolution manometry (HRM). Pharyngeal swallows were recorded with a ManoScan™ HRM in wake-upright, wake-supine, and sleep conditions in 20 healthy participants (mean 27 years; range 21–52). Velopharyngeal and hypopharyngeal segments were analysed separately. Contractile integral, mean peak pressure, inverse velocity of superior-to-inferior pharyngeal pressure, and time to first maximum pressure were analysed with custom-designed software. The supine-wake condition was compared to both upright-wake and sleep conditions using linear mixed effects models. No significant differences were found between supine-wake and upright-wake conditions on any measures. The mean peak pharyngeal pressure was lower during sleep than during the supine-wake condition for both the velopharynx (− 60 mmHg, standard error [SE] = 11, $p < 0.001$) and hypopharynx (− 59 mmHg, SE = 9, $p = 0.001$), as was the pharyngeal inverse velocity (− 12 ms/cm, SE = 4, $p = 0.012$) for the hypopharyngeal segment and the pharyngeal contractile integral (− 32 mmHg s cm, SE = 6, $p < 0.001$). No significant differences were found in time to the first pharyngeal maximum pressure. This study used HRM to characterize and compare pharyngeal pressures during swallowing in both wake and sleep conditions. No differences were found between upright and supine awake conditions, a finding important to pharyngeal manometric measures made during supine positioning, such as in fMRI. Higher pressures and longer time-related measures of volitional pharyngeal swallowing when awake indicate that cortical input plays an important role in modulation of pharyngeal swallowing.

Keywords Pharyngeal manometry · High-resolution manometry · Deglutition · Pharynx · Sleep

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Introduction

Investigating swallowing during sleep provides an important means for evaluating and understanding the reflexive swallowing response without the ambiguity of conscious control. Prior exploration of this experimental condition has centred around frequency of swallowing, rather than quantification of specific biomechanics [1–5]. While this provides important data regarding the lower frequency of swallowing during sleep of 2.9/h (SD = 1.3) [1] versus 24.4/h (SD = 8.7) when awake [6], further research is needed to characterize differences in swallowing biomechanics during wake and sleep.

Pinto et al. [7] evaluated swallowing during sleep in healthy participants ($n = 10$) and in patients with cerebral atrophy or lacunar infarct ($n = 25$). An intraluminal catheter was placed transnasally to deliver 1 mL water to the pharynx. Swallowing was measured by surface EMG (sEMG)

from the submental musculature. No difference was identified in response time to bolus presentation in controls between wake and sleep states, but 54% of the patients with neurologic impairment had a delayed swallowing response of > 5 s when asleep compared to when awake. This study was replicated with adult cats ($n = 4$) with implanted EEG and EMG electrodes [8]. Swallowing was measured with sEMG and intraluminal pharyngeal pressure, combined with an elastomer tube that provided three volumes of water (0.50 mL, 0.19 mL, 0.06 mL). While the authors concluded that swallows during wake and non-rapid eye movement sleep (NREM) conditions are similar, they also found that larger volumes of fluid produced a higher number of swallows in NREM sleep than when awake.

These studies provide early evidence to support the presence of differences in sleep swallowing beyond frequency of swallowing, with the potential for reduced accuracy in the accommodation of boluses of varying sizes due to reduced transmission of afferent sensory feedback during sleep. Changes in pharyngeal pressure measures when asleep, compared to awake, would provide additional data on the role of volition in modulating motor control of swallowing. The present study evaluated the pharyngeal swallowing response in healthy subjects during sleep and wake conditions using high-resolution manometry (HRM), with a primary aim of determining the role of volition in modulating pharyngeal swallowing. We hypothesized that normal healthy adults would produce (i) swallowing of lower pressure amplitude when asleep, suggested by prior research utilizing sEMG [1, 2], and (ii) reduced latency between maximal superior and inferior pharyngeal pressures during sleep, as prior animal research have shown reduced modulation of temporal aspects of swallowing [8].

Materials and Methods

Participants

Twenty-two healthy participants (4 males, 18 females), ranging in age from 21 to 52 years (mean = 27 years), were recruited for this study. No participant reported a history of dysphagia, neurological or muscular impairment, or use of any medications known to affect swallowing or sleep. Ethical approval was obtained from the local institutional review board, and informed consent was obtained from all participants prior to commencement of data collection.

Equipment

Participants were evaluated using the ManoScan™ HRM system (Model A120) with a 2.75-mm diameter ESO catheter (EPS0042) containing 36 solid-state pressure sensors. In vivo calibrations were routinely performed and each recording session was preceded by calibration per standard operating instructions.

Procedure

The HRM catheter was placed transnasally using a routine protocol [9, 10]. Once inserted, it was taped securely to the external nares with medical adhesive tape and the participant was provided with a few minutes to accommodate to the presence of the catheter. Each subject was asked to perform five dry swallows at a self-generated pace, approximately one swallow every minute to record baseline function. Sips of water were offered as needed to moisten the mouth throughout, although all analysed swallows were dry swallows.

To control for the influence of positioning, the participant was assisted to achieve a comfortable supine position in bed. Subjects then performed five dry swallows at a self-generated pace, approximately one swallow every minute, with sips of water available as needed. Subsequent to this, participants were left alone to fall asleep with the catheter in situ. The researchers monitored the participant through observation of live manometric recordings throughout the night, displayed on a computer monitor remotely connected to the ManoScan™ HRM computer and located in a different room to the data collection area. The study was terminated when the participant awoke the following morning or 8 h following commencement of the sleep study.

Data Analysis

Data Correction

Pharyngeal pressure data from HRM were exported and analysed post hoc with custom-designed software (MATLAB R2014a, The MathWorks Inc., Natick, MA, 2014). A notable measurement error was identified in the manometric recordings (Fig. 1) and reported in a previous study from our group [11]. It was not possible to correct this drift using the compensation methods available on the ManoScan™ software due to the extended study duration, as the standard thermal compensation method is only adequate for short (< 30 min) studies [11, 12]. Therefore, manual correction was applied.

A best fit line was generated from raw pressure data from each sensor across each study, using MATLAB. Outliers were identified as points at a distance greater than three standard deviations from the first regression model. As swallowing is infrequent during sleep, a linear regression enabled determination of baseline pressure throughout the recording, detecting swallow events as outliers. The data were refitted with the outliers excluded. The final best fit line equation was compared to zero, and

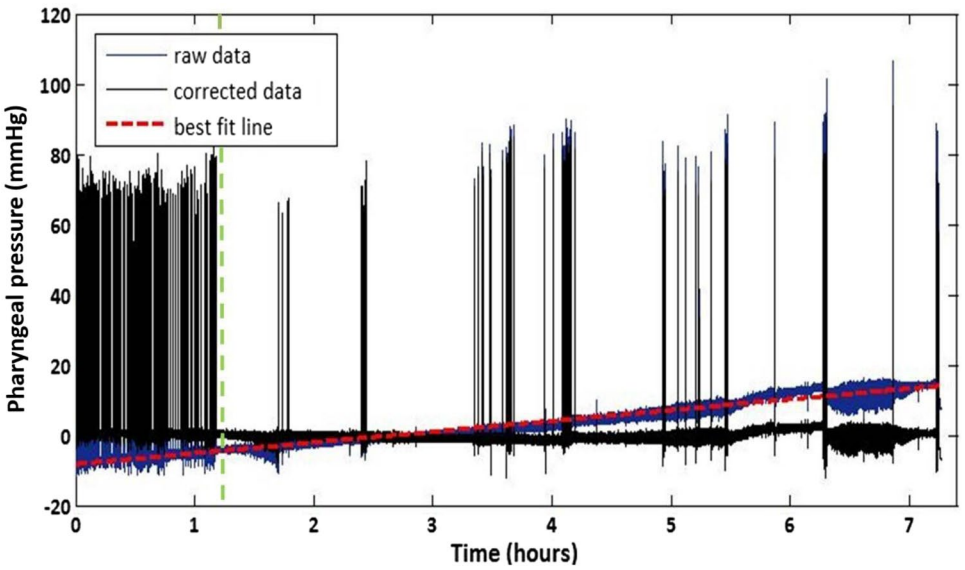

Fig. 1 An example recording from a sample sensor revealed an altered pressure at the onset of the study and an increasing measurement error over time, with deviations greater than 30 mmHg in some sensors. Raw data, corresponding to upright and supine swallows followed by the sleep swallows is plotted around the dashed best fit line [red]. All measurements of sleep swallows were commenced 1 h after the conclusion of the wake-swallowing tasks, as shown by the dashed vertical line [green]. Raw data were corrected by re-aligning the pressure to a zero baseline, as shown in black [11]

any difference from zero was subtracted from each value of raw HRM data at each time point. This levelled the baseline and manually corrected the measurement error (Fig. 1).

Data Extraction

Sensors in the velopharyngeal region were defined by at least two channels at the superior aspect of the pharyngeal spatiotemporal plot [9]. Sensors in the hypopharyngeal region were identified by selecting the sensors immediately below the velopharyngeal regions [9] and immediately above the most superior 'M-wave' channel indicative of the UES region. The sensors selected for each region were the same across all conditions (e.g., upright-wake, supine-wake, and sleep). Data were then exported for post hoc analysis with custom-designed software (MATLAB R2014a, The MathWorks Inc., Natick, MA, 2014). For each participant and condition, swallows were identified by annotating the onset of the uppermost velopharyngeal sensor and the return to baseline of the last pharyngeal sensor. All measurements of sleep swallows were commenced 1 h after the conclusion of the wake-swallowing tasks; this typically occurred approximately 2 h from the start of the recording (see Fig. 1). Any periods of the participant being awake during the night (e.g., needing the restroom) were not included in the frequency analysis. The only swallows included in this analysis were those swallows occurring with no other swallow 5 min prior and 5 min following, as prior research has identified reduction in frequency of swallowing (2.9/h (SD = 1.3) as a hallmark differentiation between sleep and wake states [2–4].

Measurements

Four measures were taken to investigate amplitude and temporal characteristics of pharyngeal swallows, with the velopharyngeal and hypopharyngeal segments analysed separately.

First, the mean pharyngeal peak pressure (mmHg) was measured by taking an average of the maximum pressure value across all sensors in each segment. Second, the inverse velocity (ms/cm) was derived, calculated as the time between peak pressure of the last sensor to peak pressure of the first sensor in each segment (e.g., velopharyngeal, hypopharyngeal), divided by the distance between these two points. Inverse velocity was preferred, as velocity necessitates discarding data when simultaneous peaks on the last and first sensors are presented (e.g., resulting in infinite velocity). Thirdly, the time to first maximum (ms) was measured, defined as the latency between the pharyngeal pressure onset to the position of the maximum pharyngeal pressure of the first pharyngeal sensor. This measure was used to investigate differences in onset of pharyngeal swallowing across conditions. Lastly, the pharyngeal contractile integral (PhCI) was derived. PhCI was calculated by creating a box that encompasses all pressures from the onset of the velopharyngeal segment to the offset of the pharyngeal segment. The mean pressure was then multiplied by the duration (s) and span (cm) within the box in units of mmHg s cm.

Statistical Analysis

Comparisons were made between upright and supine-wake measurement conditions as well as between supine-wake and supine sleep measurement conditions. Linear mixed effects

analysis was performed using R [13] and lme4 [14]. Mixed models were used as they capture the variation among the trials by modelling the variance–covariance matrix of the residuals on each measurement condition for each participant. Mixed effects allow for different numbers of trials per participant to be included, as participants had variable numbers of sleep swallows during the sleep period.

In the linear mixed effects analysis, measurement condition was entered into the model as a fixed effect with a reference category of supine-wake and intercept for subject included as a random effect. Inclusion of the by-subject random slopes for the effect of measurement condition was evaluated for the three outcome measures. The minimal adequate model was found by deletion of the by-subject random slopes from the full model. The reduced model was then compared with the full model using a likelihood ratio test. The coefficient estimates, standard error (SE), and p values of the model coefficients are reported.

Results

Feasibility and Swallowing Frequency

Two participants were unable to sleep with the catheter in situ and were excluded from analysis. The remaining participants tolerated the procedures and completed the study protocol ($n=20$). The average numbers of swallows analysed were 5.00 (SD = 0.00) for the upright and supine-wake conditions and 9.05 (SD = 4.27) for the sleep condition. Average sleep study duration was 7.6 h (range 6.9–8.2) from positioning the patient supine to the participant waking at the completion of the study. The overall swallowing frequency was 1.39 swallows/h (SD = 0.69; range 0.33–2.63) from a period of 1 h following commencement of the sleep study to the participant waking. The average lengths of the velopharyngeal and hypopharyngeal regions across participants were 1.73 cm (SD = 0.42) and 2.33 cm (SD = 0.78), respectively.

Effect of Swallowing Condition

A random intercept model was used for all the measures since the F tests of the likelihood ratios were not significant in all cases ($p>0.05$). Tables 1 and 2 summarize velopharyngeal and hypopharyngeal coefficient estimates and SE from the mixed effects model analysis for the mean peak pressure, inverse velocity, and time to first maximum for the supine-wake condition and the upright-wake and sleep conditions, respectively. All values are compared to the reference category supine-wake.

Results showed no significant differences between upright-wake and supine-wake conditions in terms of mean peak pressure (Fig. 2), inverse velocity, and time to first maximum, for neither the velopharyngeal nor the hypopharyngeal region. However, there was a difference between sleep and supine-wake conditions for mean peak pharyngeal pressure for both the velopharyngeal and pharyngeal regions, with lower mean peak pressure in the sleep condition. No significant difference for the inverse velocity measure was found between sleep and supine-wake condition in the velopharyngeal region. However, a lower inverse velocity was found for the sleep state in the pharyngeal region compared to the supine-wake condition. Finally, there were no significant differences in time to first maximum for either the velopharyngeal or pharyngeal regions for the sleep conditions when compared to supine-wake condition.

For the PhCI measure, no significant differences were found between upright-wake (65 mmHg s cm, SE = 8) and supine-wake conditions (− 2 mmHg s cm, SE = 3, $p=0.395$). The PhCI was lower during sleep than during the supine-wake condition (− 32 mmHg s cm, SE = 6, $p<0.001$).

Table 1 Velopharyngeal coefficient estimates and standard error (SE) of mean peak pressure, inverse velocity, and time to first maximum as a result of measurement condition (e.g., supine-wake, upright-wake, and sleep) with supine-wake as a reference category

Measure	Supine-wake	Upright-wake	Sleep
Mean peak pressure (mmHg)	109 (9)	2 (4) $p=0.669$	− 60 (11) $p<0.001$***
Inverse velocity (ms/cm)	97 (19)	− 8 (10) $p=0.426$	− 6 (21) $p=0.767$
Time to first maximum (ms)	295 (42)	− 57 (31) $p=0.083$	− 67 (53) $p=0.221$

Values for upright-wake and sleep indicate the estimated difference and the SE of the difference from the supine-wake condition

***$p<0.001$

Table 2 Hypopharyngeal coefficient estimates and standard error (SE) of mean peak pressure, inverse velocity, and time to first maximum as a result of measurement condition (e.g., supine-wake, upright-wake, and sleep) with supine-wake as a reference category

Measure	Supine-wake	Upright-wake	Sleep
Mean peak pressure (mmHg)	123 (6)	4 (3) $p=0.222$	− 59 (9) $p<0.001$***
Inverse velocity (ms/cm)	53 (3)	2 (2) $p=0.331$	− 12 (4) $p=0.012$*
Time to first maximum (ms)	220 (28)	− 18 (15) $p=0.223$	51 (34) $p=0.130$

Values for upright-wake and sleep indicate the estimated difference and the SE of the difference from the supine-wake condition

*$p<0.05$, ***$p<0.001$

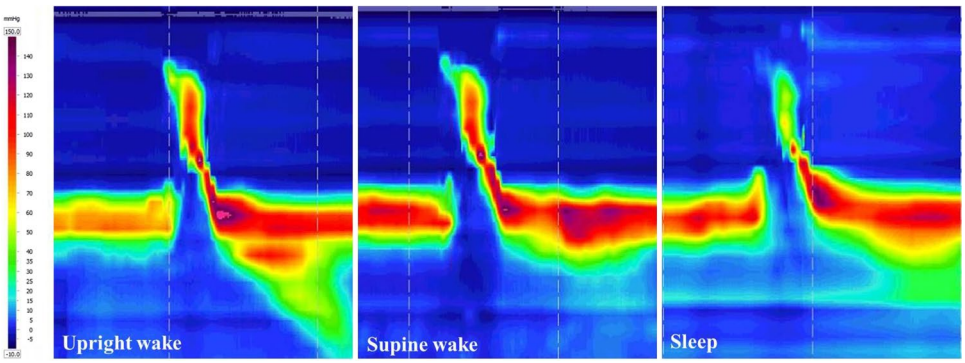

Fig. 2 Spatiotemporal HRM plots displaying one selected swallow at each of the three conditions: upright-wake, supine-wake, and sleep conditions from one subject. Sleep swallows showed a lower mean peak pharyngeal pressure than wake conditions as demonstrated by a cooler colour in the sleep swallow

Discussion

This study characterized and compared pharyngeal pressures by HRM during swallowing in both wake and sleep conditions. From a methodological perspective, 91% of healthy participants tolerated the overnight manometric procedure but two were unable to complete the study protocol due to difficulty sleeping with an intraluminal nasal catheter. Previous studies have reported tolerance of 87% ($n = 107$) [15] up to 96% ($n = 799$) [16]. The high compliance in the present study with a 2.75-mm intraluminal catheter supports the general finding that most participants are able to sleep with the catheter in place. However, larger diameter 4-mm catheters tend to be less well accepted (53%, $n = 36$) [17].

Swallowing frequency in this study was comparable with previous reports [1, 3]. Our results confirmed our hypothesis that normal healthy adults have lower-amplitude pharyngeal swallowing pressures when asleep. Markedly reduced amplitudes of velopharyngeal and hypopharyngeal pressures in sleep are consistent with reduced sEMG amplitude documented in other studies [1, 3, 5]. Results from the temporal analyses revealed a lower inverse velocity in the hypopharyngeal segment and lower PhCI during sleep compared with supine-wake swallows. It is possible that the reduction in amplitude and PhCI in sleep states relates to the reduction in salivation during sleep. However, in a study of adult cats [8], increasing the volume of administered fluid resulted in a higher number of swallows in NREM sleep, as opposed to adaptations in the magnitude and duration of swallowing observed during wakefulness on increased bolus size. This may reflect reduced accommodation to bolus sizes due to limited cortical modulation during sleep, highlighting the role of volition in modulation of swallowing pressure generation. Similar findings in previous research indicated that patients with neurologic impairment demonstrated a delay in swallowing initiation in response to bolus presentation when asleep as compared to when awake [7]. It is postulated this might be a consequence of reduced perception and response to afferent sensory feedback during sleep.

Healthy participants demonstrated no significant differences between upright and supine awake conditions in regard to amplitude or timing measures. This is important for techniques reliant on supine positioning, such as fMRI. Further studies have reported that supine positioning results in no difference from upright in terms of pharyngeal transit time [18] and timing and contraction of laryngeal adductor muscles [19].

In terms of limitations, importantly this study does not investigate possible relationships between the current findings and specific sleep stages, as EEG data were not acquired. Future studies can extend the present work by directly comparing changes in swallowing biomechanics with the different sleep stages. Extricating the influence of saliva/bolus size continues to require further exploration. Further, the manual correction of HRM used in the present study was non-standardized and future research should replicate the results using system-based correction.

Conclusion

This study provides early evidence of distinct differences in pharyngeal amplitude, inverse velocity, and PhCI when asleep compared to awake states and, in turn, emphasizes the role of cortical modulation in the execution of volitional pharyngeal swallows. Investigation of swallowing during sleep is a viable and important means for understanding the reflexive pharyngeal swallowing and the role of cortical control in modulating swallowing behaviour.

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Compliance with Ethical Standards

Conflicts of interest The authors declare they have no conflict of interest.

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