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# Swallowing and respiratory pattern in young healthy individuals recorded with high temporal resolution

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***Abstract*** *The coordination of swallowing and respiration is essential for a safe swallow. Swallowing consists of several subsecond events. To study this, it is important to use modalities with high temporal resolution. In this study, we have examined young healthy individuals with simultaneous videofluoroscopy, videomanometry and respiratory recording, all with high temporal resolution. The onset of 13 predetermined swallowing and respiratory events and the surrounding respiratory phase pattern were studied in different body positions and during different respiratory drives. An increased respiratory drive was induced by breathing 5%* $CO_2$*. The results demonstrated a highly repeatable and fixed temporal coordination of the swallowing pattern despite body position and respiratory drive. Previous studies have demonstrated a period of centrally controlled apnoea during swallowing. This apnoea period has a variable length, varying from 1 to 5 s. During increased respiratory drive, we could demonstrate a significantly shorter period of apnoea during swallowing, mainly due to an earlier resumption of respiration. The high temporal recordings in this study have revealed that swallowing during expiration is present basically in all healthy individuals. This swallowing respiratory pattern seems to be appropriate for a safe swallow. This knowledge will be used as a reference for future studies on how swallowing and respiratory coordination might be altered due to ageing and diseases.*

***Keywords*** *apnoea, coordination, resolution, respiratory, swallowing, temporal.*

**Abbreviations:** AE, apnoea end; AS, apnoea start; E-E phase, expiration before and after swallowing; E-I phase, expiration before and inspiration after swallowing; I-E phase, inspiration before and expiration after swallowing; I-I phase, inspiration before and after swallowing; PhCL, lower level of the pharyngeal constrictor; PhCM, middle level of the pharyngeal constrictor; SA, swallowing apnoea; SAD, swallowing apnoea duration; TB, tongue base; UOS, upper oesophageal sphincter.

## INTRODUCTION

The pharynx constitutes a common pathway for air, food and liquid. Therefore, a safe swallow requires a high degree of coordination with breathing to minimize the risk of laryngeal penetration and pulmonary aspiration. Several anatomic elements and functional events prevent aspiration during swallowing. Apart from these factors, there is also a period of centrally controlled swallowing apnoea (SA), i.e. respiration ceases as the bolus passes through the pharynx. The mechanism behind this centrally controlled SA and how it cooperates with swallowing has been extensively studied.[1–6]

Most swallows are preceded and followed by expiration. Swallows followed by an inspiration are rare but have been demonstrated in up to 10% of swallows.[2–7] It has been suggested that expiration following swallowing might protect the larynx from aspiration

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by clearing residue of food from the pharynx before resumption of respiration. Patients with neuromuscular disease or neurological disorders often suffer from aspiration and also have a higher frequency of swallows followed by inspiration.[8,9] However, why this unfavourable pattern also exists in healthy individuals is not known.

Swallowing and respiratory neurons are localized close together in the brain stem and have similar morphology and function.[10–13] We know that swallowing influences respiration as respiration ceases during swallowing. We also believe that respiration influences swallowing as hypercapnia has been demonstrated to increase inspirations following swallowing.[14] Thus, we know that swallowing and respiration are highly coordinated.

Even though an upright position is the normal way of feeding, it is not unusual that elderly people have to be fed in a supine position. Also, aspiration of saliva during sleep is a potential cause of aspiration pneumonia, due to oropharyngeal colonization of pathogenic bacteria.[15,16]

For further studies in this field, we believe it is important to use modalities with high temporal resolution to evaluate the interactions of these events.

The aim of this study was to define timing of respiratory and swallowing events with high temporal resolution, in young healthy volunteers, in different body positions and during different respiratory drives.

## MATERIALS AND METHODS

Thirty-two healthy volunteers were included in the study (16 men and 16 women) with a mean age of 25 years (20–35 years). None of the subjects had any history of dysphagia, gastro-oesophageal reflux disease or surgery to the pharynx, larynx or the oesophagus. None of the subjects were on any medication at the time of the study. None used tobacco. The study was approved by the Regional Ethics Committee on Human Research at the Karolinska Institute, Stockholm, Sweden and the study was performed according to the Declaration of Helsinki. Written informed consent was obtained from each study participant.

### Respiratory recording

A bidirectional air flow meter (ASF 1420; Sensirion AG, Staefa, Switzerland) was used to measure the inspiratory and expiratory oral and nasal air flow using a dual temperature compensated thermistor (CMOSens®; Sensirion AG). The sensor had an internal flow integration time of 5 milliseconds (ms). This made it possible to determine the start, end and duration of flow or apnoea (ms), as well as direction of flow (inspiration or expiration). The air flow meter is validated by comparing it with diaphragmatic and abdominal electromyography and was proved to be accurate and reliable.[17]

Furthermore, a nasal pressure transducer (RespSponse™; SynMed Medicinteknik, Spånga, Sweden) was used, which was inserted in one of the nostrils. This non-calibrated pressure transducer delivered an analogue signal that, due to variable built in time delay, was suitable for monitoring direction of flow but not the exact timing of flow and apnoea.

The oral and nasal airflow signal was Digital/Analogue converted, then digitized and sampled (Polygraf®; SynMed Medicinteknik) together with the nasal pressure signal. Using these two techniques, the respiratory events, surrounding the swallow, were recorded in relation to bolus location and pharyngeal muscle contractions (Fig. 1).

The bidirectional air flow meter was connected to the volunteer by a tightly fixed face mask. The face mask had three sealed openings and the nasal pressure transducer was introduced through one of the openings. Through the other two openings, the manometry catheter and the catheter for administration of the contrast medium were introduced.

### Manometric recording

The manometry catheter had a diameter or 4.6 mm with four solid-state pressure transducers positioned 2 cm apart. There was a 5-cm-long extension of the catheter that ended with a 5-mm radiopaque tip**.** The two proximal sensors were standard micro transducers (Konigsberg Instruments Inc., Pasadena, CA, USA) with a single recording site oriented radially to measure 120°, whereas the two distal transducers were circumferential, allowing 360° measurements. All sensors were easy to identify during fluoroscopy due to radiopaque markers. The transducer system was extremely non-compliant with a low volumetric compliance and a pressure rise rate >2000 mm of mercury per second (mmHg $s^{-1}$). The sampling frequency was 64 Hz. The analogue signal was converted to a digital signal (Polygraf®; SynMed Medicinteknik). The manometric and the respiratory registration, were superimposed on the videofluoroscopic image, using a Microeye Video Output Card (Digihurst Ltd, Roystone, UK) and displayed together on a monitor and recorded together on videotape (S-VHS).The computer was IBM compatible and the software used was the Polygram Upper-GI Edition (Gastrosoft Inc./SynMed Medicinteknik). All pressure values were expressed in mmHg. The system was calibrated at 0 mmHg and at 50 mmHg. The calibration was done at 37 °C. All given values are referred to atmospheric pressure. The manometry catheter was inserted through the nostril and positioned, fluoroscopically, with the distal tip in the proximal oesophagus and the distal transducer at the level of the upper oesophageal sphincter (UOS). The three proximal transducers were positioned at the level of the tongue base and at two different levels of the pharyngeal constrictor muscles, middle (PhCM) and lower (PhCL) level. The proximal transducers were positioned with the recording sites in a dorsal direction. During swallowing, the larynx–pharynx elevation moved the UOS cranially, so when the catheter was correctly positioned in the proximal part of the UOS, a characteristic M-shaped configuration appeared on the manometry registration.[8,18–20]

### Videofluoroscopy equipment

A Philips digital system (Multi Diagnost 4; Philips Digital System, Brest, The Netherlands) was used for fluoroscopy. Videofluoroscopic recording was done with a resolution of 50 fields (25 frames) per second. Video analysis was performed by slow motion and frame-by-frame analysis. Timing of the events was done by comparing the fluoroscopy image to the manometry registration as these were displayed on the same monitor. Timing was assessed counting frame-by-frame with a known video speed of 25 frames per second.

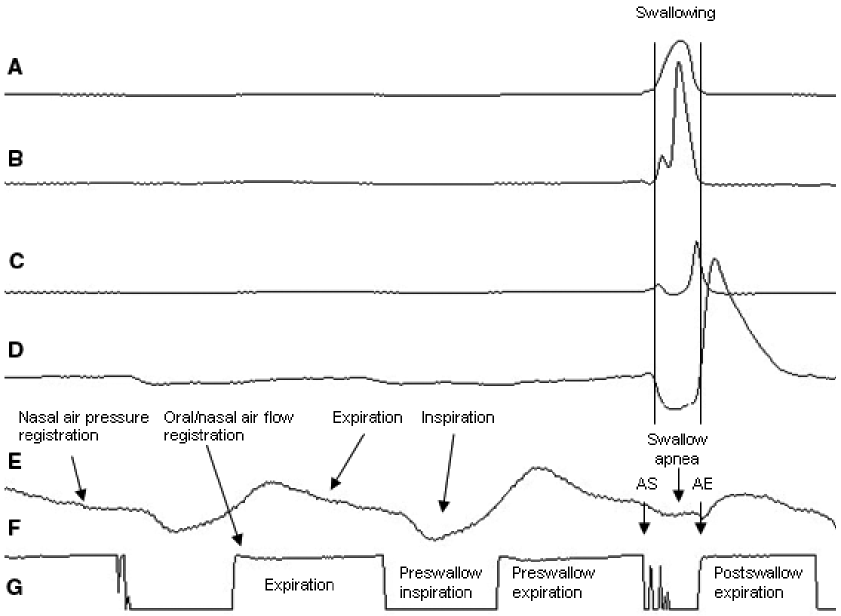

**Figure 1** Simultaneous pharyngeal manometry and respiratory registration during swallowing. The manometric registrations were done on four levels where (A) represent the tongue base level, (B) represent the middle pharyngeal constrictor level, (C) the lower pharyngeal constrictor level, and (D) the upper oesophageal sphincter level. Respiratory registration was done with two modalities where (E) represent the nasal pressure registration and (F) the oral/nasal air flow registration. On the nasal pressure registration, a positive registration indicated expiration whereas a negative registration indicated inspiration and a flat line indicated swallowing apnoea. On the oral/nasal air flow registration, an upward horizontal line indicated expiration, a downward horizontal line indicated inspiration and swallowing apnoea was indicated by an oscillating signal. AS, apnoea start; AE, apnoea end.

## Protocol

Simultaneous videoradiography, solid-state intraluminal manometry (videomanometry) and respiratory registration were performed in both the upright lateral and the left decubitus position (head of the table tilted 8–9° upward). The left decubitus position was chosen to obtain a lateral fluoroscopy image.

The volunteers were studied during three conditions:

1 *Upright* lateral position, breathing normal air, *normocapnia.*
2 *Left decubitus* position, breathing normal air, *normocapnia*.
3 *Left decubitus* position, breathing air with an addition of 5% $CO_2$, *hypercapnia*, to increase the respiratory drive by inducing hyperventilation**.**

All volunteers performed three repetitions of swallowing during each condition, starting in the upright position. Ten millilitres of water soluble contrast medium (Omnipaque® 240 mg $mL^{-1}$; Nycomed Imaging, Oslo, Norway) was given as an orally administered bolus via syringe. Subjects were informed before the contrast medium was given and instructed to swallow when comfortable.

In each participant, 13 swallowing and respiratory events were selected for analysis, to determine their exact temporal order during swallowing. We defined the start of the ventral movement of the hyoid bone as the indicator of the starting point of pharyngeal swallowing and this event was selected as the time 0 ($t_0$). All other events were then referred in time to this particular event. The 13 events are defined in Table 1.

Respiratory phase related to swallowing was measured from registration of the air flow meter (thermistor) and from the nasal pressure transducer, as described in Fig. 1. Registration from the air flow meter clearly determined the start and end of expiration and inspiration as well as apnoea start (AS) and apnoea end (AE).

Swallow–respiratory phase relationship was defined as E-E, expiration before and after swallowing, I-E, inspiration before and expiration after swallowing, E-I, expiration before and inspiration after swallowing and I-I, inspiration before and after swallowing.

Swallowing apnoea duration, SAD, was analysed and the respiratory cycle surrounding SA was analysed according to its duration and relationship to SA. To compare the durations in the upright and the left decubitus position and during normocapnia and hypercapnia, we selected only swallows with E-E phase pattern for analysis, as this was the predominant pattern. During swallows with E-E phase pattern, the respiratory cycle consists of the last inspiration preceding swallowing, the last expiration preceding swallowing and the continuing expiration after swallowing (Fig. 1).

Three respiratory durations were analysed:

**1** Preswallow inspiration duration.
**2** Preswallow expiration duration.
**3** Postswallow expiration duration.

Eleven manometric events were selected for analysis and are defined in Table 1 and Fig. 2.

Apart from the previously described temporal radiographic events (Table 1), we also analysed three radiographic events by videofluoroscopy:

**1** Premature pharyngeal spill-over, defined as the head of bolus passed the faucial isthmus more than 500 ms before the hyoid ventral excursion.
**2** Laryngeal penetration, defined as
**(i)** Subepiglottic penetration.
**(ii)** Supraglottic penetration.
**(iii)** Tracheal aspiration.
**3** Pharyngeal retention, defined as a residue of contrast material in the pharynx after ending the pharyngeal swallowing.

## Statistics

Comparisons of the manometric values, timing of swallowing and respiratory events and respiratory durations in the upright *vs* the left decubitus position and during normocapnia *vs* hypercapnia were made using ANOVA repeated measurements and presented as mean values ± standard deviation (SD) or with 95% confidence intervals (CI). The mean value of three swallows was calculated for each parameter and each individual. *P*-values <0.05 were considered statistically significant. Correlation analysis was used to calculate the correlation factors of the swallowing and respiratory events. *P*-values <0.005 were considered statistically

**Table 1** Definitions of 13 radiographic, manometric and respiratory temporal events and 11 manometric swallowing events

| Temporal events | Definitions |
|---|---|
| Radiographic temporal events | |
| Hyoid ventral ($t_0$) | First ventral movement of the hyoid bone ($t_0$) |
| Bolus at faucial isthmus | Head of bolus passed the posterior aspect of the ramus of the mandible |
| Max vestib closure | Total elimination of air contrast in the vestibular inlet |
| Bolus at vestib inlet | Head of bolus at the level of vestibular inlet |
| Bolus below UOS | The tail of the bolus have passed the upper oesophageal sphincter |
| Vestib opening | First appearance of air contrast in the vestibular inlet |
| Manometric events | |
| TB start | Start of contraction of the tongue base |
| UOS relax start | Start of relaxation of the upper oesophageal sphincter |
| PhCM start | Start of contraction of the middle pharyngeal constrictor |
| PhCL start | Start of contraction of the lower pharyngeal constrictor |
| UOS constr start | Start of contraction of the upper oesophageal sphincter |
| Respiratory temporal events | |
| Apnoea start | Last registration of stable airflow before apnoea |
| Apnoea end | First registration of stable airflow after apnoea |
| Manometric events | |
| Tongue base contraction pressure | The maximal contraction pressure (mmHg) at the tongue base level |
| Tongue base contraction duration | The duration of the contraction pressure (ms) at the tongue base level |
| Tongue base contraction rate | The raise of the contraction pressure (mmHg) per ms at the tongue base level |
| Pharyngeal contraction pressure | The maximal contraction pressure (mmHg) at the lower pharyngeal constrictor level |
| Pharyngeal contraction duration | The duration of the contraction pressure (ms) at the lower pharyngeal constrictor level |
| Pharyngeal contraction rate | The raise of the contraction pressure (mmHg) per ms, at the lower pharyngeal constrictor level |
| Tongue base–Pharyngeal muscle contraction velocity | The velocity (cm $s^{-1}$) from the maximal tongue base contraction to the maximal lower pharyngeal contraction |
| UOS relaxation duration | The duration (ms) of the UOS relaxation |
| UOS relaxation pressure | The mean pressure value (mmHg) during the UOS relaxation |
| Coordination of UOS and lower pharyngeal constrictor | The duration (ms) between the start of the lower pharyngeal contraction and the start of the UOS relaxation duration |
| UOS contraction pressure | The maxial contraction pressure (mmHg) after relaxation at the UOS level |

These 13 swallowing and respiratory temporal events are selected for analysis to determine their exact temporal order during swallowing. The start of the ventral movement of the hyoid bone was determined as an indicator for the starting point of the pharyngeal swallowing. This event has been selected as the time 0 ($t_0$). All other events were then referred in time to this particular event. Eleven manometric events evaluated in upright position, left decubitus position during normocapnia and left decubitus position during hypercapnia.

significant to avoid mass significance. STATISTICATM 7.1 (Statsoft ® Inc, Tulsa, OK, USA) was used for statistical analyses.

## RESULTS

One female was not examined in the upright position due to dizziness caused by hypotension. Eight swallows of totally 288, were excluded from analysis due to technical problems, over projection of the individuals shoulder and/or extreme oblique projections. Five registrations of respiratory duration, out of 288, were excluded from analysis due to artefacts causing interpreting difficulties.

### Temporal coordination

Correlation analyses demonstrated a well-timed coordination of the 13 events during swallowing. The closing of the vestibular inlet was correlated to the time when the bolus reached the vestibular inlet ($P < 0.005$) and the contraction start of the PhCM, PhCL and UOS were highly correlated ($P < 0.005$) and contracted subsequently in time. The AE was correlated to the vestibular opening ($P < 0,005$). However, there was no correlation of AS to any events and AS showed a high variability and often started long before swallowing (Fig. 3A).

The temporal coordination of the physiological swallowing events was stable comparing all three conditions, the upright with the left decubitus position and normocapnia with hypercapnia (Fig. 3A,B). Only the vestibular closure time was significantly earlier in the left decubitus position (−2.6 ± 69 ms, mean ± SD) compared to the upright position (28.8 ± 62 ms, mean ± SD). There were no significant differences comparing normo- and hypercapnia.

Respiratory coordination demonstrated a higher degree of variability comparing the three conditions. SAD was significantly decreased during hypercapnia

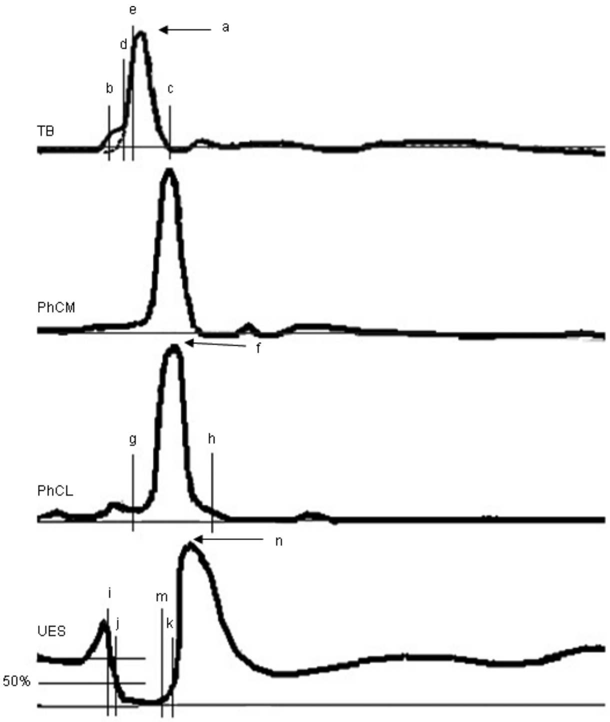

**Figure 2** Schematic of normal manometric tracings. The manometry sensors are positioned at the level of the tongue base (TB), the middle pharyngeal constrictors (PhCM), the lower pharyngeal constrictors (PhCL) and the cranial aspect of the upper oesophageal sphincter (UOS). TB contraction pressure (a) was measured as the highest pressure during TB contraction. TB contraction start (b) was measured from the first upstroke of the pharyngeal stripping wave. In case of an intrabolus pressure, an extrapolation was done from the upstroke of the contraction wave and down to the pharyngeal stripping wave. The TB contraction start is a temporal event that is measured from the first ventral excursion of the hyoid bone ($t_0$), to the start of the TB contraction. TB contraction duration (b, c) was measured as the duration from the TB start to the TB end. TB contraction rate (d, e) was measured as the raise in pressure (mmHg) from the beginning of the contraction wave to just before the peak of the contraction. This value was divided with the duration of the pressure raise (ms). PhCL contraction pressure (f) was measured as the highest pressure during PhCL contraction. PhCL contraction duration (g, h). PhCL contraction rate was measured in the same way as the tongue base contraction rate. TB–PhCL contraction velocity (a–f) was measured as cm s$^{-1}$. UOS relaxation start (i) was measured from the first relaxation of the UOS. This parameter is a temporal event that is measured from the start of the ventral excursion of the hyoid bone ($t_0$) to the start of the UOS relaxation. UOS relaxation duration (j, k) was measured from the point representing 50% of the difference between the UOS resting pressure (the pressure of the UOS between swallows) and the nadir and to the corresponding point at the UOS contraction wave. UOS relaxation pressure was measured as the mean pressure during the UOS relaxation duration (j, k). Coordination of the UOS and PhCL (g–j) was measured in ms. UOS contraction start (m) was measured from the first upstroke of the UOS stripping wave. This parameter is a temporal event that is measured from the start of the ventral excursion of the hyoid bone ($t_0$) to the start of the UOS contraction. UOS contraction pressure (n) was measured as the highest pressure during UOS contraction.

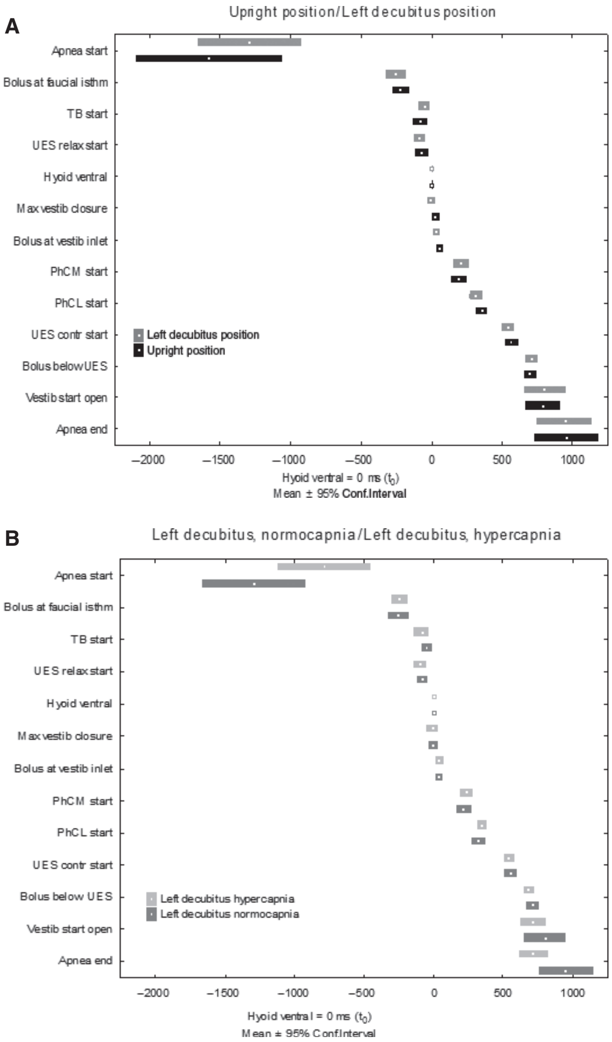

**Figure 3** Temporal coordination of swallowing and respiratory events in (A) upright and left decubitus position with normocapnia and (B) left decubitus position with normocapnia and with hypercapnia. All values are in milliseconds (ms) and are mean values ± 95% confidence interval (CI). TB, tongue base; UOS, upper oesophageal sphincter; PhCM, middle pharyngeal constrictor; PhCL, lower pharyngeal constrictor. For explanation, see Table 1.

(1495 ± 927 ms, mean ± SD) compared to normocapnia (2237 ± 1283 ms, mean ± SD, $P = 0.003$). The time of AE was significantly earlier during hypercapnia (713 ± 253 ms, mean ± SD) compared to normocapnia (945 ± 523 ms, mean ± SD, $P = 0.043$) (Fig. 3B). The timing of the AS was delayed during hypercapnia compared to normocapnia, however, this was not significant.

There were no significant differences in respiratory coordination comparing the upright and the left decubitus position (Fig. 3A).

## Swallow–respiratory phase pattern

Swallow–respiratory phase pattern was analysed in a total of 288 swallows in the upright and the left decubitus position and during normo- and hypercapnia. In this study, we demonstrated the E-E swallowing respiratory phase pattern in 286 of 288 swallows. Only in one individual, we found one I-E and one E-I swallow in left decubitus position. In all other individuals, we found only E-E swallows, in the upright and the left decubitus position as well as during normo- and hypercapnic breathing.

### Duration of respiratory phases surrounding SA

During hypercapnia, there was a significantly shorter expiration before as well as after swallowing compared to normocapnia (Table 2). There were no other significant differences in the durations of inspiration or expiration preceding or following swallowing comparing the upright and the left decubitus position or normo- and hypercapnia.

### Manometric values

The UOS contraction pressure was lower in the left decubitus position compared to the upright position and the UOS relaxation pressure (the UOS pressure between swallows) was significantly lower during hypercapnia compared to normocapnia (Table 3). None of the remaining manometric values showed any significant differences comparing the upright and the left decubitus position or during normo- and hypercapnia.

### Radiographic evaluation

Radiographic variables were analysed in a total of 93 swallows in the upright position, 95 swallows in the left decubitus position and in 92 swallows in the left decubitus position during hypercapnia. Pharyngeal spill-over was present in 10–13% of the swallows in all three conditions. Subepiglottic penetrations were present in only 2–4% of the swallows in all conditions. Only one supraglottic penetration was found in the left decubitus position during normocapnia. All penetrations were totally cleared during swallowing. Tracheal aspiration was never noticed, irrespectively of position or respiratory drive. Retention was only seen in three swallows.

## DISCUSSION

Respiratory and swallowing neurons are localized together in the brainstem.[10,11] Their interaction is of great importance for a safe swallowing. The primary objective of this study was to obtain normative data on respiratory and swallowing coordination in young healthy individuals using simultaneous modalities. The technique of airflow recordings, developed by our research group, measures both nasal and oral airflow with high temporal resolution. This made it possible to assess a precise measurement of inspiration and expiration in correlation to the exact position of contrast bolus and to the contractions and relaxations of the pharyngeal and cricopharyngeal muscles. To further challenge the interaction of swallowing and respiration, the study was designed to determine whether body position or respiratory drive influenced swallowing physiology or swallowing–respiratory coordination. This is the first in a series of studies with the aim to define normal and abnormal respiratory and swallowing patterns.

### Comparing the upright and the left decubitus position

Correlation analyses demonstrated a well-timed correlation of the respiratory and pharyngeal-laryngeal swallowing events in young healthy individuals. This is consistent with previous studies by Martin-Harris *et al.*[3,4,21] It was obvious that the timing of the swallowing and respiratory events was not changed comparing the upright and the left decubitus position.

**Table 2** Swallowing apnoea duration and durations of respiratory phases surrounding swallowing apnoea

| Position | Insp before SA (ms) | Expir before SA (ms) | Expir after SA (ms) | SAD (ms) |
|---|---|---|---|---|
| Upright | 1468 ± 541 | 1727 ± 1243 | 1644 ± 568 | 2535 ± 1630 |
| Left decubitus during normocapnia | 1333 ± 333 | 1335 ± 786 | 1525 ± 753 | 2237 ± 1283 |
| Left decubitus during hypercapnia | 1194 ± 374 | 988 ± 623* | 1158 ± 383* | 1495 ± 927* |

Mean duration ± SD of swallowing apnoea duration (SAD) and of expirations (expir) and inspirations (inspir) preceding and following swallowing apnoea (SA), in a total of 283 swallows in 30 individuals. During hypercapnia, there was a significantly shorter expiration as well before ($P = 0.03$) as after swallowing ($P = 0.02$) compared to normocapnia. SAD was significantly shorter during hypercapnia compared to normocapnia ($P = 0.003$).

**Table 3** Eleven manometric events were evaluated in upright position and in left decubitus position with normo- and hypercapnia

| Eleven manometric events | Upright position | Left decubitus position | Left decubitus position with $CO_2$ |
|---|---|---|---|
| TB contraction pressure (mmHg) | 288 ± 132 | 287 ± 111 | 283 ± 134 |
| TB contraction rate (mmHg s$^{-1}$) | 1430 ± 793 | 1525 ± 758 | 1464 ± 792 |
| TB contraction duration (ms) | 778 ± 165 | 736 ± 148 | 717 ± 155 |
| PhCL contraction pressure (mmHg) | 298 ± 119 | 286 ± 124 | 257 ± 100 |
| PhCL contraction rate (mmHg s$^{-1}$) | 1404 ± 476 | 1347 ± 535 | 1511 ± 946 |
| PhCL contraction duration (ms) | 568 ± 134 | 559 ± 99 | 512 ± 78 |
| TB–PhCL contraction velocity (cm s$^{-1}$) | 12.6 ± 4.4 | 13.2 ± 5.9 | 12.9 ± 3.4 |
| UOS relaxation duration (ms) | 583 ± 153 | 593 ± 134 | 575 ± 131 |
| UOS relaxation pressure (mmHg) | 14.7 ± 11.4 | 15.1 ± 10.5* | 9.5 ± 10.6* |
| Coordination of UOS relaxation and PhCL contraction (ms) | −311 ± 122 | −277 ± 143 | −311 ± 118 |
| UOS contraction peak (mmHg) | 402 ± 99* | 365 ± 87* | 349 ± 84 |

Comparing the upright and left decutitus position, the UOS contraction pressure was significantly higher in the upright position ($P = 0.02$). Comparing normo- and hypercapnia, the UOS relaxation pressure was significantly lower during hypercapnia ($P = 0.000$).
TB, tongue base; PhCL, lower part of the pharyngeal constrictor; UOS, upper oesophageal sphincter.

In both positions, several respiratory and swallowing events were highly correlated to each other, with one exception, the AS. Fig. 3A shows the temporal mean values ± 95% CI. The AS was highly variable with a range from 50 to 5000 ms prior to the pharyngeal swallow. In several individuals, AS occurred while, and even before, loading the bolus into the oral cavity. AS always occurred before pharyngeal swallowing and vestibular closure, in both the upright and the left decubitus position, which is consistent with previous studies.[3,4] This implies that AS is not due to vestibular closure and indicates strongly that the AS is controlled from the brainstem.[1,3,4,22–24] The AE, though, was only correlated with one swallowing event in the upright position, i.e. the opening of the vestibular inlet. In the upright and the left decubitus position, the vestibular inlet always opened before the AE, indicating that even the AE is centrally controlled and not due to laryngeal opening. The time between the swallowing events was stable comparing the two positions except for the vestibular closing time, which occurred earlier in the left decubitus position compared to the upright position. The left decubitus position might imply an increased risk for aspiration why an early closing of the vestibulum likely would ensure a safer swallow.

The timing of the respiratory events was less stable and we could see a tendency of shortening of the SAD in the decubitus position compared to the upright position, however, this difference was not significant. McFarland *et al.*[25] demonstrated that swallows tended to occur late in the expiratory phase in the upright position and early in the expiratory phase in the 'hands and knees' position. In our study, we could not confirm this finding. The most reasonable explanation for these different findings might be due to the difference in position where the down posture in McFarland's study was on hands and knees, which might influence coordination of swallowing and respiration. Different methodology might also explain the different findings.

Consistent with previous studies,[2–5,7,25,26] we demonstrated that swallowing was initiated during expiration and the predominant respiratory phase pattern was the E-E pattern. In contrast to other studies, we could demonstrate the E-E pattern to occur in basically all swallows irrespectively of position or respiratory drive. This fits with the theory that exhalation clears the vestibular inlet from residue before the next inspiration and therefore diminishes the risk of aspiration.

Previous studies have demonstrated an incidence of I-E swallows varying from 18% to 22%.[4,6,21,24,27] When evaluating the respiratory phases, we occasionally found the preswallow expiration to be very short (Fig. 3). Saito *et al.*[28] demonstrated how stimulation of the sensory superior laryngeal nerve in rat resulted in swallowing, only if done during expiration or immediately after inspiration. If this is true for humans, we assume this indicates that swallows only can occur during expiration and accordingly, the respiratory phase patterns I-E and E-I in fact represent an E-E pattern. Thus, when the respiratory episodes are extremely short, registration with high temporal resolution is required (Fig. 4). We believe that these short expirations have been hidden in the preceding inspiration when using equipment with lower temporal resolutions.

During suckle feeding in preterm infants, the initial feeding efforts are characterized by the periods of apnoeic suckle feeding.[29] In term infants and with further development, respiration is integrated in the feeding episode and the respiratory phase changes from

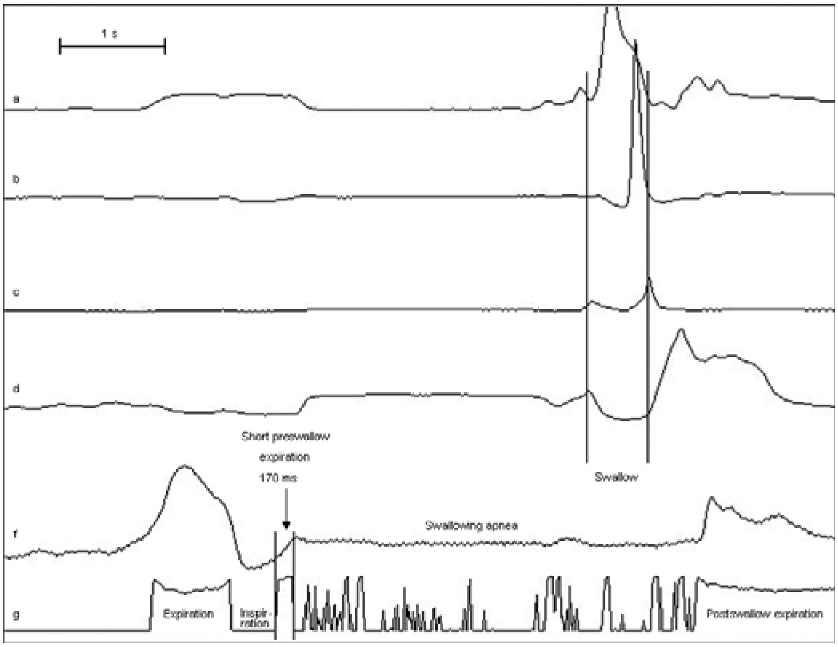

**Figure 4** Simultaneous pharyngeal manometry and respiratory registration during swallowing. The manometric registrations were done on four levels where (A) represent the tongue base level, (B) the middle pharyngeal constrictor level, (C) the lower pharyngeal constrictor level, and (D) the upper oesophageal sphincter level. Respiratory registration was done with two modalities where (E) represent the nasal pressure registration and (F) the oral/nasal air flow registration. On the oral/nasal air flow registration, a short preswallow expiration (170 ms) is indicated. This short expiration is difficult to assess from the nasal pressure registration.

E-I to I-E swallows. With further maturation and without suckle feeding, the E-E respiratory phase becomes the predominant.

When comparing manometric values in the upright and the left decubitus position, the only variable that significantly changed was the UOS contraction pressure, which was significantly lower in the left decubitus position. We know from previous studies[30,31] that the resting pressure of the UOS decreases over time. However, the described decrease of the UOS contraction pressure in the left decubitus position compared to the upright position has not been previously reported.

## Comparing normo- and hypercapnia

Comparing normo- and hypercapnia, the timing and correlation of the swallowing events were highly stable. In contrast, respiratory events surrounding the swallowing varied. AE occurred significantly earlier during hypercapnia compared to normocapnia, almost simultaneously with the closing of the UOS and the opening of the vestibular inlet. Even the SAD was significantly shorter during hypercapnia compared to normocapnia (Fig. 3B). It is reasonable, though, to believe that during hypercapnia with increased $p\text{CO}_2$, it is of great importance to prevent long periods of SA as this increases the $p\text{CO}_2$ even more. This might demonstrate how respiratory neurons interact with swallowing neurons in the brainstem, and shorten the SAD to maximize ventilation and lower the $p\text{CO}_2$. However, as the AE occurs much closer to the UOS closing time, this might alter the safety of swallowing.

Consistent with our result in the upright and the left decubitus position, the E-E phase pattern was the predominating pattern even during hypercapnia, with 100% E-E swallows. This is in sharp contrast with the studies by Nishino and Sai.[14,32] They demonstrated an increased incidence of I-I and E-I swallows during continuous infusion of water into the pharynx along with increased hypercapnia. They also demonstrated an increased incidence of coughing during hypercapnia, supporting the theory that the I-I and E-I swallows might predispose for aspiration. However, Issa and Porotstocky[33] could not demonstrate an increased incidence of coughing or aspiration during continuous infusion of water into the mouth during progressive hypercapnia. There is no obvious explanation for these different findings. Nishino has suggested that the methodological differences might be one explanation. The way of reaching hypercapnia might influence the upper airway physiology. However, the difference between our observations and that of Nishinos and Sai may be related to the different equipment for respiratory registrations, where very short expirations and inspirations might be difficult to assess, using techniques with lower temporal resolution. Using continuous infusion of water, causing continuous swallowing might have a different effect on respiratory coordination than a single bolus swallowing. In addition, presenting the water by oral infusion instead of pharyngeal infusion might give additional sensory input from the mouth and tongue, which might alter the respiratory coordination.

As described above, the SAD is shorter during hypercapnia compared to normocapnia and, accordingly, increasing the risk of aspiration. Consequently, we speculate that even during hypercapnia the E-E swallow is preferred as this is the safest swallow. This would fit with the theory that swallowing and respiratory neurons work to compensate for external influences that might challenge a safe swallow.

During hypercapnia, we demonstrated a shortening of the expiration duration before as well as after SA, this in accordance with a shorter respiratory cycle induced by the hypercapnia.

During hypercapnia, we demonstrated a significantly lower UOS relaxation pressure compared to normocapnia. As described above, the SAD is shorter during hypercapnia and AE is earlier, thus closer to the UOS closing time. This shortening of time for a 'safe bolus passage' may partially be compensated for by a decreased UOS relaxation pressure that would facilitate the bolus passage through the pharynx. Thus, the risk for residual bolus in the vestibular region and possible aspiration would be reduced.

## CONCLUSION

We found that the temporal coordination of swallowing and respiration in healthy individuals is well timed and highly stable and basically all swallows occur during an E-E pattern.

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## COMPETING INTERESTS

The authors have no competing interests.

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