Suppression of Abdominal Motor Activity during Swallowing in Cats and Humans

Teresa Pitts1*, Albright G. Gayagoy2, Melanie J. Rose2, Ivan Poliacek2, Jillian A. Condrey2, M. Nicholas Musslewhite2, Tabitha Y. Shen2, Paul W. Davenport2, Donald C Bolser2

1 Department of Neurological Surgery, Kentucky Spinal Cord Injury Research Center, University of Louisville, Louisville, KY, United States of America, 2 Department of Physiological Sciences, University of Florida, Gainesville, FL, United States of America

* t.pitts@louisville.edu

Abstract

Diseases affecting pulmonary mechanics often result in changes to the coordination of swallow and breathing. We hypothesize that during times of increased intrathoracic pressure, swallow suppresses ongoing expiratory drive to ensure bolus transport through the esophagus. To this end, we sought to determine the effects of swallow on abdominal electromyographic (EMG) activity during expiratory threshold loading in anesthetized cats and in awake-healthy adult humans. Expiratory threshold loads were applied to recruit abdominal motor activity during breathing, and swallow was triggered by infusion of water into the mouth. In both anesthetized cats and humans, expiratory cycles which contained swallows had a significant reduction in abdominal EMG activity, and a greater percentage of swallows were produced during inspiration and/or respiratory phase transitions. These results suggest that: a) spinal expiratory motor pathways play an important role in the execution of swallow, and b) a more complex mechanical relationship exists between breathing and swallow than has previously been envisioned.

Introduction

The precise coordination of breathing and swallowing plays an important role to prevent entrance of food and other materials into the lower respiratory tract. Diseases which effect pulmonary mechanics such as chronic obstructive pulmonary disease (COPD), and or lung tumors result in changes to the coordination of swallow and breathing [1–3]. COPD is one of the thirteen statistically significant influencing factors that were implicated in the development of aspiration pneumonia [3–7]. Additionally, patients with COPD swallow more often during inspiration and consequently are at increased risk for post-swallow aspiration events [8, 9]. This disrupted breathing/swallow pattern could increase the risk of aspiration in patients with advanced COPD and may contribute to exacerbations [10, 11].

Expiratory threshold loading is an experimental technique which reliably elicits abdominal recruitment in human [12–20] and animal models [21–25]. A 15 cm H2O expiratory threshold load increases rectus abdominis, internal oblique, transverses abdominis and gastric pressure...
to approximately 5–30% of maximum activity produced during cough [26]. Previous work [27] has increased our understanding of the interaction of swallow with other airway protective behaviors, and pressure threshold loading allows for the testing of its interaction with active expiration.

Pitts et al [28] proposed a dual valve system composed of highly coordinated control of both the laryngeal adductor and upper esophageal sphincter in regulating pressures between upper airway and the thoracic cavity, which controls the passage of air/bolus into or out of the lungs and esophagus. During swallowing, the pressure differential produced by upper esophageal relaxation and the maximal activity of tongue and pharyngeal muscles propels the bolus into the esophagus. During the expiratory phase of breathing, requirements for the production of swallowing are low because trans-laryngeal flows (i.e. air movement through the larynx) and intra-thoracic pressures are minimal. However, in patients with alterations in respiratory mechanics leading to increases in intra-thoracic pressure, such as with abdominal muscle recruitment, dysphagia may be promoted by hindrance of bolus movement across the upper esophageal sphincter.

The aims of this study were to determine if swallowing and breathing are coordinated during active expiration and if swallows affect pressure regulation by altering laryngeal and respiratory muscle activity. We hypothesized that swallows increase the duration and decrease the maximal activity of expiratory muscles during expiratory loading.

Methods

Animal Model

Approval for this study was granted from the University of Florida Institutional Animal Care and Use Committee (IACUC). The experiments were performed on six spontaneously breathing adult cats (5.2 ± 1.1 kg), obtained from Liberty Research, Inc, and housed at the University of Florida. The animals were anesthetized with sodium pentobarbital (35–40 mg/kg iv) and additional doses were given as needed (1–3mg/kg iv). The right femoral vein was cannulated for intravenous drugs administration and the right femoral artery was accessed for arterial blood sampling and blood pressure monitoring. A tracheostomy was performed and a cannula was inserted to allow spontaneous breathing. Arterial blood pressures, arterial blood gasses, end tidal CO₂, and vital signs were monitored. An esophageal balloon was placed via an oral approach to measure pressure in the mid-thoracic esophagus. A rectal temperature probe was inserted to allow maintenance of body temperature at 37±1°C.

Electromyograms were recorded using bipolar insulated fine wire electrodes according to the technique of Basmajian and Stecko [29]. Seven muscles were used to evaluate breathing and swallowing: swallowing muscles (mylohyoid, geniohyoid, thyrohyoid, thyropharyngeus, and cricopharyngeus), inspiratory muscle (parasternal), and expiratory muscle (internal oblique). The muscles were identified through surgical dissection and visual inspection followed by electrode placement. The geniohyoid was exposed through a small incision on the rostral portion of the right mylohyoid. The thyroarytenoid electrodes were inserted through the cricothyroid window near the anterior portion of the vocal folds. The thyropharyngeus was spotted as a fan shaped muscle the wires are placed at the caudal portion at the thyroid cartilage attachment. At the posterior aspect of the larynx, the cricopharyngeus was identified and electrodes were placed just cranial to the edge of this structure. Thyrohyoid muscle electrodes were inserted rostral to its attachment to the thyroid cartilage. The parasternal muscle electrodes were placed on the third intercostal space adjacent to the sternum. Expiratory muscle electrodes were placed in the internal oblique muscle. The external oblique was moved without dissection to identify the internal oblique muscle. The positions of all electrodes were confirmed
by electromyogram activity patterns during breathing and swallowing. Animals were euthanized by an overdose of sodium pentobarbital, followed by 3cc’s of potassium chloride.

**Protocol**

A non-rebreathing valve was placed on the tracheal cannula. An expiratory threshold load of 15 cmH2O was applied by attaching a hose to the expiratory port of this valve and immersing the end of the hose in a reservoir of water. Each load was 5 minutes in duration with the swallow trials beginning at the 2 minute mark. Swallow stimulation was completing by injecting 3 ml of water into the oropharynx via a syringe; this was repeated three times separated 1 minute. The swallows were identified from: a) a quiescence of the cricopharyngeus (UES), and b) overlapping large burst of activity of the mylohyoid, geniohyoid, thyropharyngeus, thyrohyoid, thyroarytenoid and the parasternal.

All EMG signals were amplified, filtered (200–5000 Hz), rectified, and integrated (time constant 50 ms). The inspiratory phase (T_I), and the expiratory phase (T_E) durations were measured. T_I was defined as the onset of parasternal activity to the maximum burst of the parasternal EMG, T_E was defined as the maximum burst of the parasternal EMG to the onset of the parasternal EMG activity for the next breath. The control (load-only) respiratory cycle durations (T_I and T_E) were compared to cycles which contained a swallow. The maximum amplitude of the inspiratory muscles (parasternal) and expiratory muscles (internal oblique) were compared to cycles which contained a swallow.

**Human Model**

Approval for this study was granted from the University of Florida Institutional Review Board (UF-IRB). All subjects provided written consent following the UF-IRB approved procedure. Five young (20 ± 1 years old) healthy males were recruited for this study. They had an average weight of 157 ± 42 pounds, height of 67 ± 3 inches, and a body mass index of 24 ± 7. All participants reported no history of swallow disorders, respiratory disease, and/or smoking within the last 10 years. The Institutional Review Board at the University of Florida approved the study.

Surface EMGs were affixed to the skin above the submental (including mylohyoid, geniohyoid and diaphragmatic) muscle group and the abdominal wall (lateral to the right rectus abdominis) over the oblique and transverses complex. To optimize abdominal recruitment all subjects were kneeling upright during the duration of the study. Subjects were asked to breathe through an apparatus comprised of a non-rebreathing valve, expiratory pressure threshold device (EMST 150, Aspire Products LLC), and a pressure transducer. The EMST 150 is a calibrated, one-way spring-loaded valve which has been used in studies for expiratory muscle strength training [12–19]. The pressure transducer confirmed the expiratory pressure necessary to overcome the load. A nose clip was affixed to ensure all airflow was through the oral cavity. During preliminary experiments, participants exposed to load significantly decreased their respiratory rate. For this set of experiments participants were asked to maintain their resting breathing rate during the loading paradigm, this decreased the need for larger expiratory threshold loads to record EMG abdominal recruitment.

**Protocol**

The EMST150 was attached to the expiratory port of the non-rebreathing valve, placed into the subject’s mouth, and slowly the expiratory threshold level was increased until respiratory phasic abdominal EMG activity was observed (30–45 seconds in duration). Following this a 3cc syringe filled with sterile water with a one-inch tubing, was slid into the participants mouth (by the investigator) and slowly the water was infused over a 20 second time-period (0.15 ml/
The subjects were instructed to “swallow when you feel it is necessary”. A five minute rest was given between each trial, and this was repeated 3 times.

For comparison all EMG amplitude measures are expressed as a percentage of the largest EMG amplitude. Results are expressed as means ± standard error. For statistical analysis Student’s paired t-tests were used to identify differences. A statistical difference was considered significant if the p-value was less than 0.05.

Results

Animal Model

The loading protocol recruited active abdominal activity in all animals (Fig 1). Fig 1a demonstrates an abdominal motor unit in the 3 respiratory cycles preceding a swallow and depression of the motor unit in the cycle containing a swallow and subsequent cycles. Note, for this analysis only single swallows which had 3 respiratory cycles preceding and following the swallow were included in this analysis, for a total of 25 swallows.

The maximum abdominal EMG activity in expiratory phase, which contained a swallow (55 ±12), was significantly lower that control expiratory cycles (95±2; p = 0.02); additionally, durations of T1 which contained a swallow (5.2±0.8 s) were significantly longer than those under the control condition (3.6±0.5 s; p = 0.04). The average time from the onset of the load to expiratory recruitment was 32 ± 13 s. Sixty percent (15 of 25) of swallows occurred during the expiratory phase with the remaining 40% (10 of 25) during inspiration. We did not observe swallows occurring during a respiratory phase. Fig 1b is a line graph demonstrating each animal’s averaged data for three cycles preceding the swallow and 4 cycles following the swallow.

The maximum parasternal EMG activity in inspiratory cycles, which contained a swallow (128±15) was higher but not significantly different to that during the inspiratory control cycles (94±2; p = 0.07). The duration of TI which contained a swallow (1.2±0.3 s) was not significantly different than that under the control condition (1.0±0.08 s; p = 0.4) (Table 1).

There was no significant difference in the maximum EMG for swallows during the control versus the loading condition: mylohyoid (p = 0.6), geniohyoid (p = 0.3), thyrohyoid (p = 0.4), thyropharyngeus (p = 0.7), cricopharyngeus (p = 0.7), thyroarytenoid (p = 0.2), and parasternal (p = 0.5). All eighty swallows were included in this analysis, regardless of the respiratory phase in which they occurred.

Human Model

The loading protocol recruited active abdominal activity in all subjects, which could be detected by surface EMG. The analysis included 54 swallows, and all subjects produced at least one swallow during the inspiratory phase of breathing. Fig 2 demonstrates abdominal suppression during an expiratory phase containing a swallow. Note the abdominal EMG burst, at the beginning of the expiratory cycle, is due to the active expiration required to open the pressure threshold load valve, to allow airflow. The maximum abdominal surface EMG activity of expiratory phases, which contained a swallow (64±8), was significant lower than that during the expiratory control phases (90±1; p = 0.02). The submental surface EMG amplitude (79±9) and duration was not significantly different for swallows during the loading condition (84±3; p = 0.29).

During the control condition 57 ± 11% of swallows occurred during the expiratory phase, with 5 ± 4% during the inspiration-expiratory transition, and 38±11% during the expiratory to inspiratory transition. However, during the loading condition 11 ± 9% of swallows occurred during the inspiratory phase, with a reduction of their occurrence during the expiratory phase (29 ± 14). Additionally 7 ± 6% of swallows occurred during the inspiratory-expiratory phase.
transition and the largest percentage (53 ± 15) occurred during the expiratory-inspiratory phase transition. Duration measurements were not obtained for the human measures. As noted previously, the subjects voluntarily constrained their respiratory frequency to the control rate. This instruction allowed for smaller expiratory threshold loads to be applied and increased subject compliance.

Fig 1. A. Example of abdominal motor unit suppression with swallow. Note the positive wave on the esophageal pressure channel. This is indicative of the peristaltic wave during the esophageal phase of swallow. Swallow is denoted by the arrow, the first 2 cycles occurred on the inspiratory-expiratory phase transition, the third is during the inspiratory phase of breathing. B. Line graph depicting average change in abdominal EMG amplitude for each of the five animals. N denotes the expiratory cycle that contained the swallow, n-1 to n-3 are the three preceding expiratory cycles, and n+1 to n+4 are the four following expiratory cycles. Four of the five animals had evidence of a multi-cycle suppression. For this analysis only single swallows which had 3 respiratory cycles preceding and following the swallow were included in this analysis.

doi:10.1371/journal.pone.0128245.g001
This is the first report of swallow suppressing the active abdominal recruitment during expiratory threshold loading in humans and cats. As seen in previous research: a) the expiratory threshold loading protocol increased abdominal EMG activity [14, 17, 21]; and shifted swallow from occurring predominately during expiration to inspiration [10, 11]. However, the present results demonstrate a more complex coordination system for breathing and swallow. Swallow has classically been thought of as a brainstem reflex that is produced solely by cranial and upper cervical motoneuron pools [30, 31]. Our results suggest that motoneuron pools in the thoracic and lumbar spinal cord also participate in the production of this behavior. Bautista, et al [32] in the perfused brainstem preparation of juvenile rats has also showed suppression of abdominal activity, however not as significant as was seen during the inspiratory phase of eupnoea. A limitation of the perfused brainstem preparation, is that there is no lung/thoracic phasic sensory feedback during breathing. Their findings, along with ours suggest that abdominal suppression by swallowing is a nascent feature of the core central pattern generator for swallow.

Both, our human subjects and experimental animals were unparalyzed, raising the possibility that peripheral feedback related to the mechanical changes that occur during a swallow.

Table 1.

A. Respiratory EMG changes

| Amplitude (% Maximum) | Load | Load + Swallow | P value |
|-----------------------|------|----------------|---------|
| Cat                   |      |                |         |
| Parasternal           | 70 ± 7 | 93 ± 3         | 0.07    |
| Rectus Abdominis      | 95 ± 1 | 45 ± 7         | <0.001  |
| Human                 |      |                |         |
| Abdominal             | 90 ± 1 | 64 ± 8         | 0.02    |

B. Swallow EMG changes

| Amplitude (% Maximum) | Rest Breathing | With Load | P value |
|-----------------------|----------------|-----------|---------|
| Cat                   |                |           |         |
| Mylohyoid             | 76 ± 8         | 73 ± 6    | 0.6     |
| Geniohyoid            | 65 ± 20        | 76 ± 7    | 0.3     |
| Thyrohyoid            | 76 ± 18        | 85 ± 4    | 0.4     |
| Thyropharyngeus       | 63 ± 11        | 61 ± 16   | 0.7     |
| Cricopharyngeus       | 59 ± 17        | 65 ± 19   | 0.7     |
| Thyroarytenoid        | 74 ± 18        | 85 ± 6    | 0.2     |
| Parasternal           | 47 ± 9         | 49 ± 11   | 0.5     |
| Human                 |                |           |         |
| Submental             | 73 ± 9         | 84 ± 3    | 0.3     |

*Significant P < 0.05

Changes to inspiratory and expiratory EMG amplitude and duration comparing cycles with expiratory loading and expiratory loading with swallow. B. Changes to laryngeal, pharyngeal, and schluckatmung EMG amplitude during control swallows (rest breathing) and swallows during expiratory threshold loading.

doi:10.1371/journal.pone.0128245.t001
could influence this larger depression in abdominal motor activity, seen in the present study. If so, the afferent sources likely arise from thoracic-abdominal somatic and/or visceral mechano-receptors. A central source for these effects is also possible, consisting of depression of bulbospinal excitatory drive to abdominal motoneuron pools during swallow. Abdominal motoneuron pools receive their excitatory drive during breathing from expiratory phasic premotoneurons in the region of caudal nucleus reticularis, also known as the caudal ventral respiratory column [33].

Active expiratory suppression theoretically affected pressures across the upper esophageal sphincter to enhance bolus propulsion during swallowing. Negative intra-esophageal pressure during swallow has been described in humans [34–36] and animals [28, 37–40]; here referred to as the “schluckatmung” a German word meaning “swallow breath” [41–44]. McConnell has also published a series of papers describing this as the “hypopharyngeal suction pump” [45–59]. The source of this pressure has been disputed with two leading theories: a) phrenic nerve activity driving diaphragm activity [60, 61], or b) elevation of the laryngeal complex [46, 47, 58, 59]. It could also result from the combination of these two forces to create the necessary negative pressure. With the necessity of an adequate intra-esophageal pressure formation during swallow, now aligns swallow more with “inspiration during breathing” and the knowledge of lung mechanics can be applied.

During swallow, bolus movement is ensured by the combination of positive pressure (from the tongue/oral/velopharyngeal cavity), negative pressure (from the diaphragm and other accessory inspiratory muscles), along with pharyngeal squeezing which propels the bolus into the esophagus. However, even more important is the creation of a positive-negative pressure differential from the upper airway into the esophagus. Disorders such as COPD and lung cancer (large tumors) could create resting intra-thoracic pressures, with patient’s using active

---

Fig 2. An example of swallowing in a young healthy male, and the abdominal suppression across the entire expiratory period. Note the small burst of abdominal activity at the beginning and the larger burst of abdominal activity at the end of the expiratory period was the consistent pattern.

doi:10.1371/journal.pone.0128245.g002
abdominal recruitment during the expiratory phase of breathing, which results in a mechanical disadvantage for execution of swallowing. This mechanical disadvantage could be overcome with multiple strategies including: suppression of ongoing active abdominal recruitment during swallows occurring during the expiratory phase of breathing, and/or shifting swallow phase to inspiration (as seen in these results), which would move the occurrence of swallow to the respiration phase with the greatest negative intrathoracic pressure.

A larger percentage of swallows were produced during inspiration or phase transitions in our experiments than are normally reported during control conditions [27, 39, 40, 62–65]. However, it is unknown whether the phase preference and phase shift during loading is a solely central/brainstem mediated phenomenon, or if continuous feedback from chest-wall, vagal, and/or abdominal afferents regulate swallow occurrence during active expiration. Additionally, during expiratory threshold loading there was no significant change in EMG amplitude in the laryngeal or pharyngeal muscles. This implies that pharyngeal activity is not necessarily subject to chestwall feedback; rather it is respiratory muscle motor control that is altered to promote bolus transfer. This is different than what was seen during the coordination of coughs and swallows in the cat; in which all pharyngeal and laryngeal muscle activity were significantly increased. This may represent a more delineated response to changes in respiratory status based on alterations in expiratory drive, which is significantly greater during cough than loading [21].

In summary, swallow breathing interactions are more complex than previously appreciated. Active expiratory suppression is an airway protective mechanism which should ensure than an adequate differential pressure is created across the upper esophageal sphincter. In conditions which modify respiratory mechanics, such as COPD and lung cancer, this may represent a significant strategy for maintaining the integrity of the bolus to ensure safe eating.

Author Contributions
Conceived and designed the experiments: TP AGG MJR IP JAC MNM PWD DCB. Performed the experiments: TP AGG MJR IP JAC MNM DCB. Analyzed the data: TP AGG TYS. Contributed reagents/materials/analysis tools: TP PWD DCB IP. Wrote the paper: TP AGG IP JAC MNM TYS PWD DCB.

References
1. Clayton NA, Carnaby GD, Peters MJ, Ing AJ. Impaired laryngopharyngeal sensitivity in patients with COPD: The association with swallow function. International journal of speech-language pathology. 2014. Epub 2014/02/26. doi: 10.3109/17549507.2014.882987 PMID: 24564527.
2. Tsuzuki A, Kagaya H, Takahashi H, Watanabe T, Shiyo T, Sakakibara H, et al. Dysphagia causes exacerbations in individuals with chronic obstructive pulmonary disease. Journal of the American Geriatrics Society. 2012; 60(8):1580–2. Epub 2012/08/15. doi: 10.1111/j.1532-5415.2012.04067.x PMID: 22889024.
3. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. Journal of the American Medical Directors Association. 2011; 12(5):344–54. doi: 10.1016/j.jamda.2010.12.009 PMID: 21450240
4. Hibberd J, Fraser J, Chapman C, McQueen H, Wilson A. Can we use influencing factors to predict aspiration pneumonia in the United Kingdom? Multidisciplinary respiratory medicine. 2013; 8(1):Article number 39.
5. Taylor JK, Fleming GB, Singanayagam A, Hill AT, Chalmers JD. Risk Factors for Aspiration in Community-acquired Pneumonia: Analysis of a Hospitalized UK Cohort. The American journal of medicine. 2013; 126(11):995–1001. doi: 10.1016/j.amjmed.2013.07.012 PMID: 24054176
6. Vaishnavi A, Satia I, Balasubramanian D, Sundar R. S64 Understanding better the pathophysiology of aspiration pneumonia. Thorax. 2011; 66(Suppl 4):A31–A2. PMID: 22191100
7. Pace CC, McCullough GH. The association between oral microorganisms and aspiration pneumonia in the institutionalized elderly: review and recommendations. Dysphagia. 2010; 25(4):307–22. doi:10.1007/s00455-010-9298-9 PMID: 20824288
8. Singh B. Impaired swallow in COPD. Respirology. 2011; 16(2):185–6. doi:10.1111/j.1440-1843.2010.01903.x PMID: 21077991
9. Martin-Harris B, McFarland DH. Coordination of Deglutition and Respiration. Principles of Deglutition: Springer; 2013. p. 25–34.
10. Cvejic L, Harding R, Churchward T, Turton J, Finlay P, Massey D, et al. Laryngeal penetration and aspiration in individuals with stable COPD. Respirology. 2011; 16(2):269–75. doi:10.1111/j.1440-1843.2010.01875.x PMID: 21054669
11. Terramot S, Kume H, Ouchi Y. Altered swallowing physiology and aspiration in COPD. CHEST Journal. 2002; 122(3):1104–5. PMID:12226067
12. Kim J, Sapienza CM. Implications of expiratory muscle strength training for rehabilitation of the elderly: Tutorial. J Rehabil Res Dev. 2005; 42(2):211–24. PMID: 15944896.
13. Bolser DC, Reier PJ, Davenport PW, Bolser DC. Expiratory muscle strength training in persons with multiple sclerosis having mild to moderate disability: effect on maximal expiratory pressure, pulmonary function, and maximal voluntary cough. Arch Phys Med Rehabil. 2006; 87(4):468–73. PMID: 16571384.
14. Wheeler KM, Chiara T, Sapienza CM. Surface electromyographic activity of the submental muscles during swallow and expiratory pressure threshold training tasks. Dysphagia. 2007; 22(2):108–16. PMID: 17294298.
15. Pitts T, Bolser D, Rosenbek J, Troche M, Okun MS, Sapienza C. Impact of expiratory muscle strength training on voluntary cough and swallow function in Parkinson disease. Chest. 2009; 135(5):1301–8. Epub 2008/11/26. chest.08-1389 [pii] doi:10.1378/chest.08-1389 PMID: 19029430.
16. Troche M, Okun M, Rosenbek J, Musson N, Fernandez H, Rodriguez R, et al. Aspiration and swallowing in Parkinson disease and rehabilitation with EMST. Neurology. 2010; 75(21):1912–9. doi:10.1212/WNL.0b013e3181fef115 PMID: 21098406.
17. Goldstein I, Goldstein S, Urbanetti J, Anthonisen N. Effects of expiratory threshold loading during steady-state exercise. Journal of applied physiology. 1975; 39(5):697–701. PMID: 1184506.
18. Bolser DC, Reier PJ, Davenport PW. Responses of the anterolateral abdominal muscles during cough and expiratory threshold loading in the cat. J Appl Physiol. 2000; 88(4):1207–14. Epub 2000/04/06. PMID: 10749809.
19. Jammes Y, Bye PT, Pardy RL, Katsardis C, Esau S, Roussos C. Expiratory threshold load under extracorporeal circulation: effects of vagal afferents. Journal of applied physiology: respiratory, environmental and exercise physiology. 1983; 55(2):307–15. Epub 1983/08/01. PMID: 6413463.
20. Jammes Y, Bye PT, Pardy RL, Roussos C. Vagal feedback with expiratory threshold load under extracorporeal circulation. Journal of applied physiology: respiratory, environmental and exercise physiology. 1983; 55(2):316–22. Epub 1983/08/01. PMID: 6225756.
21. Leevers AM, Road JD. Some effects of vagal blockade on abdominal muscle activation and shortening in awake dogs. J Physiol. 1995; 488 (Pt 2):471–81. Epub 1995/10/15. PMID: 8568685; PubMed Central PMCID: PMC1156685.
28. Pitts T, Rose MJ, Mortensen AN, Poliacek I, Sapienza CM, Lindsey BG, et al. Coordination of cough and swallow: A meta-behavioral response to aspiration. Respiratory Physiology & Neurobiology. 2013.

29. Basmajian J, Stecko G. A new bipolar electrode for electromyography. Journal of Applied Physiology. 1962; 17(5):849.-

30. Jean A. Control of the central swallowing program by inputs from the peripheral receptors. A review. Journal of the autonomic nervous system. 1984; 10(3–4):225–33. Epub 1984/05/01. PMID: 6384335.

31. Jean A. Brain stem control of swallowing: neuronal network and cellular mechanisms. Physiological Review. 2001; 81(2):929–69. PMID: 11274347.

32. Bautista TG, Dutschmann M. Ponto-medullary nuclei involved in the generation of sequential pharyngeal swallowing and concomitant protective laryngeal adduction in situ. The Journal of physiology. 2014; 592(12):2605–23. doi:10.1113/jphysiol.2014.272468 PMID: 24639482

33. Iscoe S. Control of abdominal muscles. Progress in neurobiology. 1998; 56(4):433–506. Epub 1998/10/17. PMID: 9775401.

34. Hårdemark Cedborg AI, Sundman E, Bodén K, Hedström HW, Kuylenstierna R, Ekberg O, et al. Coordination of spontaneous swallowing with respiratory airflow and diaphragmatic and abdominal muscle activity in healthy adult humans. Experimental Physiology. 2009; 94(4):459–68. doi:10.1113/expphysiol.2008.045724 PMID: 19139059

35. Wilson S, Thach B, Brouillette R, Abu-Osba Y. Coordination of breathing and swallowing in human infants. Journal of Applied Physiology. 1981; 50(4):851. PMID:7263368

36. Hunt P, Connell A, Smiley T. The cricopharyngeal sphincter in gastric reflux. Gut. 1970; 11(4):303–6. PMID: 5428852

37. Hellemans J, Vantrappen G. Electromyographic studies on canine esophageal motility. Digestive Diseases and Sciences. 1967; 12(12):1240–55. PMID: 6075724

38. Bonis J, Neumueller S, Marshall B, Krause K, Qian B, Pan L, et al. The effects of lesions in the dorsolateral pons on the coordination of swallowing and breathing in awake goats. Respiratory Physiology and Neurobiology. 2011; 175(2):272–82. doi: 10.1016/j.resp.2010.12.002 PMID: 21145433

39. Feroah TR, Forster H, Fuentes CG, Lang IM, Beste D, Martino P, et al. The effects of spontaneous swallows on breathing in awake goats. Journal of Applied Physiology. 2002; 92(5):1923–35. PMID:11960942

40. Feroah TR, Forster H, Fuentes CG, Wenninger J, Martino P, Hodges M, et al. Contributions from rostral medullary nuclei to coordination of swallowing and breathing in awake goats. Journal of Applied Physiology. 2002; 93(2):581–91. PMID:12133868

41. Starling E. Überblick über den gegenwärtigen Stand der Kenntnisse über die Bewegungen und die Innervation des Verdauungskanals. Ergebnisse der Physiologie, biologischen Chemie und experimentellen Pharmakologie. 1902; 1(2):446–65.

42. Vantrappen G, Hellemans J. Studies on the normal deglutition complex. Digestive Diseases and Sciences. 1967; 12(3):255–66. PMID:6019220

43. Nishino T. The swallowing reflex and its significance as an airway defensive reflex. Frontiers in physiology. 2011; 3:489-.

44. Kennedy JG III, Kent RD. Physiological substrates of normal deglutition. Dysphagia. 1988; 3(1):24–37. PMID: 3073916

45. Cerenko D, McConnel FM, Jackson RT. Quantitative assessment of pharyngeal bolus driving forces. Otolaryngol Head Neck Surg. 1989; 100(1):57–63. Epub 1989/01/01. PMID: 2493617.

46. Ku DN, Ma PP, McConnel FM, Cerenko D. A kinematic study of the oropharyngeal swallowing of a liquid. Annals of biomedical engineering. 1990; 18(6):655–69. Epub 1990/01/01. PMID: 2281886.

47. McConnel FM. Analysis of pressure generation and bolus transit during pharyngeal swallowing. Laryngoscope. 1988; 98(1):71–8. Epub 1988/01/01. doi: 10.1288/00005537-1988801000-00015 PMID: 3336265.

48. McConnel FM, Cerenko D, Hersh T, Weil LJ. Evaluation of pharyngeal dysphagia with manofluorography. Dysphagia. 1988; 2(4):187–95. Epub 1988/01/01. PMID: 3075168.

49. McConnel FM, Cerenko D, Jackson RT, Guffin TN Jr. Timing of major events of pharyngeal swallowing. Arch Otolaryngol Head Neck Surg. 1988; 114(12):1413–8. Epub 1988/12/01. PMID: 3190869.

50. McConnel FM, Cerenko D, Jackson RT, Hersh T. Clinical application of the manofluorogram. Laryngoscope. 1988; 98(7):705–11. Epub 1988/07/01. doi: 10.1288/00005537-1988707000-00003 PMID: 3386373.

51. McConnel FM, Cerenko D, Mendelsohn MS. Manofluorographic analysis of swallowing. Otolaryngol Clin North Am. 1988; 21(4):625–35. Epub 1988/11/01. PMID: 3196295.
52. McConnel FM, Guffin TN Jr, Cerenko D. The effect of asymmetric pharyngoesophageal pressures on manofluorographic measurements. Laryngoscope. 1991; 101(5):510–5. Epub 1991/05/01. doi: 10.1288/00005537-199105000-00012 PMID: 2030630.

53. McConnel FM, Guffin TN Jr, Cerenko D, Ko AS. The effects of bolus flow on vertical pharyngeal pressure measurement in the pharyngoesophageal segment: clinical significance. Otolaryngol Head Neck Surg. 1992; 106(2):169–74. Epub 1992/02/11. PMID: 1738549.

54. McConnel FM, Hester TR, Mendelsohn MS, Logemann JA. Manofluorography of deglutition after total laryngopharyngectomy. Plastic and reconstructive surgery. 1988; 81(3):346–51. Epub 1988/03/01. PMID: 3340668.

55. McConnel FM, Hood D, Jackson K, O'Connor A. Analysis of intrabolus forces in patients with Zenker's diverticulum. Laryngoscope. 1994; 104(5 Pt 1):571–81. Epub 1994/05/01. PMID: 8189989.

56. McConnel FM, Mendelsohn MS, Logemann JA. Examination of swallowing after total laryngectomy using manofluorography. Head & neck surgery. 1986; 9(1):3–12. Epub 1986/09/01. PMID: 3623931.

57. McConnel FM, Mendelsohn MS, Logemann JA. Manofluorography of deglutition after supraglottic laryngectomy. Head & neck surgery. 1987; 9(3):142–50. Epub 1987/01/01. PMID: 3623944.

58. McConnel FM, O'Connor A. Dysphagia associated with pharyngoesophageal segment dysfunction. Acta oto- laryngologica Belgica. 1994; 48(2):157–63. Epub 1994/01/01. PMID: 8209678.

59. Mendelsohn MS, McConnel FM. Function in the pharyngoesophageal segment. Laryngoscope. 1987; 97(4):483–9. Epub 1987/04/01. PMID: 3561135.

60. Howard P, Pryde A, Heading R. Oesophageal manometry during eating in the investigation of patients with chest pain or dysphagia. Gut. 1988; 30(9):1179–86. PMID: 2806985.

61. Negus V. The second stage of swallowing. Acta Otolaryngol (suppl)(Stockh). 1948; 49(78):79–82.

62. Martin-Harris B, Brodsky MB, Price CC, Michel Y, Walters B. Temporal coordination of pharyngeal and laryngeal dynamics with breathing during swallowing: single liquid swallows. Journal of Applied Physiology. 2003; 95(5):1735. PMID: 12506044

63. Wheeler Hegland K, Huber JE, Pitts T, Davenport PW, Sapienza CM. Lung Volume Measured During Sequential Swallowing in Healthy Young Adults. Journal of Speech, Language, and Hearing Research. 2011; 54(3):777. doi: 10.1044/1092-4388(2010-09-0237) PMID: 20966381

64. Wheeler Hegland KM, Huber JE, Pitts T, Sapienza CM. Lung volume during swallowing: single bolus swallows in healthy young adults. Journal of Speech, Language, and Hearing Research. 2009; 52 (1):178. doi: 10.1044/1092-4388(2008/07-0165) PMID: 18723599

65. Dick T, Oku Y, Romaniuk J, Cherniack N. Interaction between central pattern generators for breathing and swallowing in the cat. The Journal of Physiology. 1993; 465(1):715.