



The Role of the Cerebellum in Control of Swallow: Evidence of Inspiratory Activity During Swallow

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Abstract

Anatomical connections are reported between the cerebellum and brainstem nuclei involved in swallow such as the nucleus tractus solitarius, nucleus ambiguus, and Kölliker-fuse nuclei. Despite these connections, a functional role of the cerebellum during swallow has not been elucidated. Therefore, we examined the effects of cerebellectomy on swallow muscle recruitment and swallow–breathing coordination in anesthetized freely breathing cats. Electromyograms were recorded from upper airway, pharyngeal, laryngeal, diaphragm, and chest wall muscles before and after complete cerebellectomy. Removal of the cerebellum reduced the excitability of swallow (i.e., swallow number), and muscle recruitment of the geniohyoid, thyroarytenoid, parasternal (chestwall), and diaphragm muscles, but did not disrupt swallow–breathing coordination. Additionally, diaphragm and parasternal muscle activity during swallow is reduced after cerebellectomy, while no changes were observed during breathing. These findings suggest the cerebellum modulates muscle excitability during recruitment, but not pattern or coordination of swallow with breathing.

Introduction

The pharyngeal phase of swallow requires pharyngeal afferent feedback to initiate precise sequential muscle coordination to move a bolus from the oral cavity through the esophagus [1]. Additionally, swallow is highly coordinated with a host of other airway-protective behaviors including breathing, cough, vomiting and speech (i.e. [2]). While the mechanisms which regulate this coordination is not entirely understood, the cerebellum has been implicated [3–5].

Most animal studies designed to investigate the role of the cerebellum on ingestion are focused on feeding behavior where stimulating portions of the fastigial nucleus can evoke swallow-like movements [6, 7]. However, there are no readily identified studies investigating the contribution of cerebellar nuclei to swallow motor pattern or coordination with airway-protective behaviors. Changes to other reflexes such as baroreception, hypercapnic/hypoxia, and cough reflexes have been reported following lesions to the cerebellar fastigial nuclei as well as complete cerebellectomy [8–10]. Similar to these other behaviors, swallow also involves sensory integration and pattern generation at the level of the nucleus tractus solitarius (NTS) [1, 11]. Further, anatomical connections between the cerebellum and nuclei involved in swallow such as the NTS, nucleus ambiguus, and Kölliker-fuse nuclei also have been reported [1, 12, 13].

Despite clear evidence for connections between the cerebellum and swallow-related nuclei, a distinct functional role for the cerebellum during swallow has remained elusive. Therefore, the goal of this study was to investigate changes in swallow motor pattern and swallow–breathing coordination after cerebellectomy. We hypothesized that removal of the cerebellum would reduce the recruitment of pharyngeal, laryngeal, and inspiratory swallow muscles, and alter swallow phase preference during breathing.

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Methods

Experiments were performed on eight spontaneously breathing adult male cats (4.285 ± 0.9 kg). The protocol was approved by both the University of Florida and University of Louisville Institutional Animal Care and Use Committees (IACUC). The animals were initially anesthetized with sodium pentobarbital (Lundbeck, Inc., Deerfield, IL) (35 mg/kg i.v.); supplementary doses were given as needed (1–3 mg/kg i.v.). The right femoral artery and vein were cannulated to monitor blood pressure and administer fluids IV, respectively, and a tracheostomy was performed. Physiologic levels of end-tidal CO₂ (4–4.5%; Datax Engstrom; Datax Ohmeda, Inc; Madison, WI), body temperature (Homeothermic Blanket Control Unit; Harvard Apparatus; Holliston, MA), and arterial blood gas composition (i-STAT1; Abaxis; Union City, CA) were continually monitored and maintained [2].

Electromyograms (EMGs) were recorded using bipolar-insulated fine wire electrodes (A-M Systems stainless steel #791050) according to the technique of Basmajian and Stecko [14]. Eight muscles were used to evaluate swallow: mylohyoid (MyHy), geniohyoid (GeHy), thyrohyoid (ThHy), thyropharyngeus (ThPh), thyroarytenoid (ThAr), parasternal (PS), and costal diaphragm (Dia). Esophageal pressure was measured by placing a balloon catheter connected to a pressure transducer (TA-100; CWE, Inc; Ardmore, PA) into the esophagus. Both EMG placement and detection of swallow were conducted as previously described [2, 15]. Swallow was induced by introducing 3 ccs of water into the pharynx via a 1-in. long, thin polyethylene catheter (outer diameter 0.5–1.0 mm) attached to a syringe (2–3 trials were performed prior to and after cerebellectomy).

Cerebellectomy

Lidocaine was used to locally block the articular nerves (2%; 2 mg/kg), then animals were placed in a stereotaxic frame and a craniotomy exposing the cerebellum and base of the brainstem was performed. A complete cerebellectomy was performed, and the surface of the brainstem covered with warm paraffin oil.

Data Processing and Statistical Analysis

Electromyograms were recorded and analyzed using “Spike 2” Version 7 (Cambridge Electronic Design, United Kingdom). EMGs were rectified and moving averages with the time constant of 50 ms were obtained. Durations were measured between the onset and the point where the signal returned to baseline (ms). EMG amplitude measures

and esophageal pressure recordings were normalized to the largest swallow or breath and are presented as % of maximum.

A mean \pm standard error was calculated for each animal, and then averaged for each condition across animals. For statistical analysis paired *t* tests were performed between pre- versus post-cerebellectomy for the amplitude, duration and pressure measures. To assess respiratory parameters, sections of at least 40 s prior to water trials were analyzed before and after cerebellectomy. To assess swallow–breathing coordination, a Wilcoxon Signed Rank Test was used. An assigned coding system was used for the breathing phase in which the swallow occurred: inspiration (I; start to peak Dia activity) as “1”; early expiration (E1; peak to end Dia activity) as “2”; and late expiration (E2; end of Dia activity to start of next breath Dia activity) as “3”. For all tests a difference was considered significant if the *P* value was less or equal to 0.05.

Results

Cerebellectomy Reduces Swallow-Related Motor Recruitment But Does Not Disrupt Swallow–Breathing Coordination

A total of 37 water trials were conducted (17 pre-cerebellectomy, 20 post-cerebellectomy). Following cerebellectomy the GeHy, and ThAr reduced in amplitude during swallowing (Table 1; Fig. 1). Similarly, the durations of the upper airway (GeHy) and laryngeal adductor (ThAr) activity were reduced. However, the overall duration of swallow (start of MyHy activity to the end of ThPh activity) did not change. While no changes in the sequence of muscle activations were observed, the number of swallows per trial decreased (Table 1). There was no significant change in swallow–breathing coordination (Fig. 2).

Cerebellectomy Reduces Amplitude of Inspiratory Muscles During Swallow (Schluckatmung), But Not Breathing

Removal of the cerebellum produced differential effects on both the PS and Dia during swallow compared to breathing. The amplitude of the PS and Dia during swallow reduced and was coincident with a reduction in esophageal pressure (Table 1; Fig. 1). Additionally, the duration of PS activity was reduced during swallow. Conversely, PS and Dia activity did not show significant changes in amplitude during breathing, and no changes in breathing phase duration (I, E1, E2), cycle duration, or frequency were observed.

Table 1 Swallow and breathing amplitude and duration measurements before and after cerebellectomy

	Pre-cerebellectomy	Post-cerebellectomy	<i>P</i> value
Amplitude (% of max) ^a			
Mylohyoid (MyHy)	75 ± 4	58 ± 12	0.25
Geniohyoid (GeHy)	80 ± 3	45 ± 11	0.02
Thyrohyoid (ThHy)	73 ± 8	62 ± 11	0.39
Thyroarytenoid (ThAr)	87 ± 4	46 ± 13	0.03
Thyropharyngeus (ThPh)	71 ± 4	52 ± 12	0.23
Parasternal (PS; swallow)	64 ± 3	21 ± 4	< 0.01
Diaphragm (Dia; swallow)	65 ± 4	29 ± 6	< 0.01
Esophageal pressure (swallow)	− 52 ± 6	− 16 ± 7	0.01
Parasternal (PS; breathing)	63 ± 6	54 ± 10	0.43
Diaphragm (Dia; breathing)	63 ± 9	76 ± 8	0.48
Duration (ms)			
Mylohyoid (MyHy)	609 ± 21	558 ± 20	0.11
Geniohyoid (GeHy)	545 ± 26	456 ± 31	0.02
Thyrohyoid (ThHy)	483 ± 38	450 ± 27	0.58
Thyroarytenoid (ThAr)	536 ± 34	450 ± 37	0.03
Thyropharyngeus (ThPh)	549 ± 39	481 ± 40	0.07
Parasternal (PS; swallow)	624 ± 68	503 ± 64	0.03
Diaphragm (Dia; swallow)	482 ± 34	444 ± 25	0.23
Total swallow ^b	684 ± 45	640 ± 56	0.17
Inspiration (I)	902 ± 244	737 ± 114	0.32
Early expiration (E1)	615 ± 146	409 ± 51	0.10
Late expiration (E2)	1239 ± 223	1781 ± 390	0.18
Respiratory cycle ^c	2762 ± 467	2928 ± 506	0.60
Swallows/water trial	3.4 ± 0.3	2.5 ± 0.4	0.03
Respiratory rate/min	26 ± 4	26 ± 4	0.98

Mean data (± standard error) for swallow and breathing data (*n* = 8) were compared using paired *t* tests between pre- and post-cerebellectomy

P values < 0.05 are in bold

^aEMGs and esophageal pressures were normalized to the maximum EMG/esophageal amplitude

^bOnset of mylohyoid activity to offset of thyropharyngeus activity

^cOnset of I phase to offset of E2 phase

Discussion

To our knowledge, this is the first report on the impact of cerebellectomy on the excitability of the pharyngeal phase of swallow. Our results demonstrated a decrease in maximum EMG of the GeHy (by 35%), ThAr (by 41%), PS (by 43%) and Dia (by 36%); and a reduction in the duration of GeHy (by 89 ms), ThAr (by 86 ms), and PS (by 121 ms) muscles during swallow. Additionally, the number of swallows decreased following removal of the cerebellum (3.4 to 2.5 per trial), and no change in swallow–breathing coordination was observed. Of significance is the differential effect of cerebellectomy on PS and Dia muscles during swallow and breathing. While there was a reduction in PS and Dia amplitude during swallow, no significant changes were observed during breathing.

Cerebellar Involvement in Phrenic and Intercostal Muscle Recruitment During Swallow and Breathing

The involvement of inspiratory muscles during swallow (termed the schluckatmung) has been reported in humans and animals (i.e., [11, 16]). However, observations of the schluckatmung can vary by investigator and methodology. McConnel and colleagues [17] postulated that the tongue force and negative esophageal deflection has the largest impact on movement of the bolus through the esophagus. They further hypothesized that the “initial negative deflection” during the pharyngeal phase of swallow is achieved by the elevation of the larynx and opening of the upper esophageal sphincter (UES). We previously proposed, with strong supportive data, that similar to breathing, inspiratory activity during swallow creates negative pressure in the thoracic cavity thought to assist with bolus movement toward

Fig. 1 Removing the cerebellum reduces amplitude of upper airway and inspiratory muscles during swallow. Integrated EMG traces of the mylohyoid (MyHy), geniohyoid (GeHy), thyrohyoid (ThHy), thyroarytenoid (ThAr), thyropharyngeus (ThPh), parasternal (PS), and diaphragm (Dia) were made during swallows before and after the cerebellum was removed. Note the reduced amplitude of GeHy, ThAr, PS, Dia, and esophageal pressure during swallow after cerebellectomy. Scales are the same for each trace and arrows in PS and Dia denote the schluckatmung

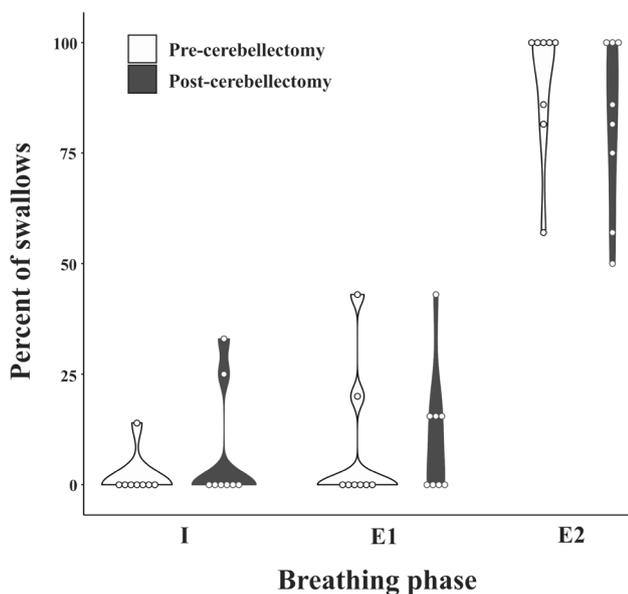
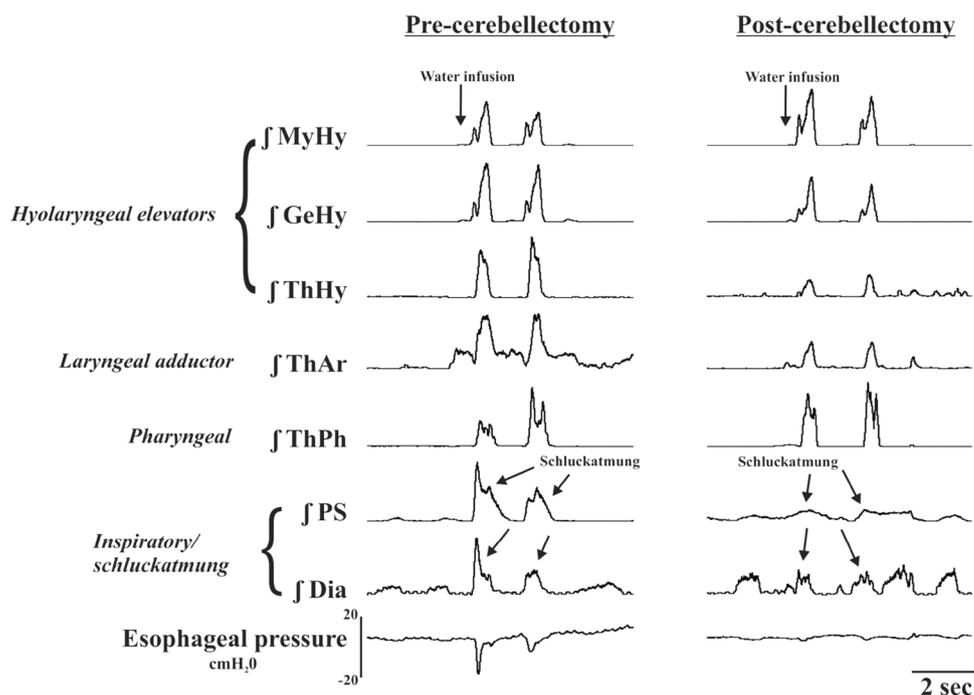


Fig. 2 Swallow–breathing coordination does not change following removal of the cerebellum. Swallows occurred during all three phases of breathing: inspiration (I), early expiration (E1), and late expiration (E2). The percent of swallows occurring during these respiratory phases was not significantly altered after cerebellectomy. Each circle represents mean data/phase from one animal

the esophagus [11, 18]. Here, we demonstrate that removal of the cerebellum also reduces the amplitude of inspiratory muscle activity during swallow (Table 1; Fig. 1).

Cerebellar involvement during breathing has been reported by a number of investigators (reviewed by [12]). Changes in both the frequency and amplitude of muscular responses related to breathing can be evoked by electrical or chemical stimulation to the fastigial nucleus of cats and rats [12]. However, breathing is largely unchanged after removal of the cerebellum under normal conditions [9]. Similarly, we did not observe significant changes to respiratory rate, duration, or amplitude of respiratory muscles following removal of the cerebellum (Table 1). Functionally, the differential effects of cerebellectomy on inspiratory muscle recruitment during swallow and breathing invite interesting questions regarding the connections between the cerebellum and multiple nuclei responsible for these two behaviors.

While it is unknown whether swallow and breathing share common inspiratory muscle pre-motor neurons, the opposing effects of cerebellectomy suggest at least some functional separation. The cerebellum projects too many brainstem sites that influence the motor control of both swallow and breathing including: nucleus tractus solitarius (NTS), the nucleus ambiguus (NA), and Kölliker fuse nuclei [1, 12, 13]. Additionally, it has recently been shown that the majority of inspiratory neurons in the NTS (part of the dorsal respiratory group) also are active during swallow [11]. Each of these nuclei also have been shown to send efferent projections to the phrenic motor nucleus in cats [19]. As such, it is possible these nuclei (perhaps specifically the NTS) drive phrenic motoneurons during swallow, independent of their effect on these same motoneurons during breathing.

Cerebellar Involvement in Swallow–Breathing Coordination and Pharyngeal/Laryngeal Recruitment

In the current study, we show that removal of the cerebellum generally results in a significant decrease in the amplitude and duration of the geniohyoid and thyroarytenoid muscles during swallow (Fig. 1; Table 1). Additionally, although the number of swallows was reduced, no difference in swallow breathing coordination was observed. These findings are consistent with response attenuation following cerebellar removal in other acute reflex behaviors involving the NTS, such as the baroreceptor reflex [8], hypercapnic/hypoxia reflex [9], and cough reflex [10]. However, both blood pressure and breathing during normal conditions are not disrupted. Our data suggest that, such as the responses to baroreception, hypercapnia, hypoxia, and cough stimuli, removal of the cerebellum reduces general excitability of the swallow reflex. As the NTS is a common pathway for these behaviors, it is likely the cerebellum modulates swallow excitability through direct connections to the NTS.

Conclusion

Here, we present data demonstrating that swallow is modulated, in part, by the cerebellum. This work adds to the growing body of literature suggesting that multiple sites and levels of the nervous system impact swallow. Importantly, questions regarding the cerebellum's specific role(s) in muscle recruitment and activity level during swallow are raised. Clinical reports have also demonstrated that diseases such as spinocerebellar atrophy can have serious swallow complications [20]. These data provide important information demonstrating that the cerebellum is involved in swallow, and is a potential pathological mechanism underlying dysphagia in some neurodegenerative diseases. Future studies which examine the effects of discrete manipulations of cerebellar nuclei and tracts are likely to further our understanding of the cerebellum's contributions to swallow.

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Compliance with Ethical Standards

Conflict of interest There are no conflicts of interest to declare.

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