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The capacity for volitional control of pharyngeal swallowing in healthy adults

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HIGHLIGHTS

- Participants can reduce temporal latency of pharyngeal pressure when swallowing.
- Reductions were correlated with changes in swallowing duration and amplitude.
- Findings may be from altering cumulative rather than discrete pharyngeal elements.
- Results suggest the pharyngeal sequence cannot be altered to pathologic levels.

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ABSTRACT

Introduction: Previous research has documented that pressure and duration of brainstem-generated pharyngeal swallowing can be cortically modulated. But there is a commonly held belief that the sequence of pharyngeal pressure remains constant. However, Huckabee et al. [19] reported a patient cohort who demonstrated reduced latency of peak pressure in the proximal and distal pharynx, disproportionate and sometimes inversely correlated with overall swallowing duration, suggesting independent timing of underlying muscle contraction within the overall pharyngeal response. This study examined if healthy adults can volitionally produce altered latency of pharyngeal closure in isolation following intensive training, thereby evaluating the capacity for pharyngeal adaptation in a healthy system.

Method: Six healthy participants were seen for intensive training, consisting of daily one-hour sessions over two weeks (10 days) using pharyngeal manometry as a visual biofeedback modality. The participants were instructed to produce simultaneous pressure in the pharyngeal sensors when swallowing. The temporal separation of peak proximal and distal pharyngeal pressure was measured with discrete-sensor pharyngeal manometry at baseline, during training with biofeedback, and following training without biofeedback.

Results: Following intensive training, participants were able to reduce temporal separation of peak pressure between the proximal and distal pharyngeal sensors from a baseline median of 188 ms (IQR = 231 ms) to 68 ms (IQR = 92 ms; $p = 0.002$). In contrast, there was no significant change in overall swallowing duration during training ($p = 0.41$). However, change in pharyngeal pressure latency was moderately correlated with both change in swallowing duration ($r = 0.444$) and amplitude ($r = 0.571$) during training, and there was a reduction in swallowing duration post-training ($p = 0.03$).

Conclusion: Given intensive manometric biofeedback training, participants substantially reduced temporal separation of peak proximal and distal pharyngeal pressure when volitionally swallowing. However, correlation with overall pressure and duration measures suggest the adaptation was one of modulating the cumulative pharyngeal response rather than altering discrete components of timing of pharyngeal pressure in isolation. This is inconsistent with the pattern of behaviour documented by Huckabee et al. [19] in the patient population. Further research on modulatory control over targeted aspects of the pharyngeal swallow is needed, and may provide avenues for rehabilitative treatment of patients with dysphagia.

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1. Introduction

The rhythmic pharyngeal phase of swallowing is controlled by a central pattern generator (CPG) formed through interconnections between the nucleus tractus solitarius (NTS) and the nucleus ambiguus (NA) in the medulla [1,22]. This understanding is based on a series of animal studies, where patterned and replicable timing of the pharyngeal swallow has been evoked, even in decerebrate animals [7,9,21,29]. Historically, it has been accepted that few parameters of swallowing are amenable to volitional alteration. For example, Ertekin [8] states "the regions of the cortex and subcortical areas involved with swallowing serve mainly to trigger deglutition and to control the beginning of the motor sequences (i.e., mainly the oral phase of swallowing). After this, sequential muscle activation is carried out without any further cortical control to perform the pharyngeal and oesophageal phases" ([8], p. 183). Over time, however, further understanding of modulatory cortical influence on the central pattern generator (CPG) driven pharyngeal swallow has suggested a greater capacity for pharyngeal change [2,13,14,18,28].

Research using techniques such as fMRI have contributed evidence that a complex array of cortical structures, including the insular, primary motor and primary sensory cortices are activated during pharyngeal swallowing [3,26]. A complex relationship between cortical and bulbar structures may allow the capability to volitionally alter select parameters of swallowing, such as strength and duration, in response to peripheral afferent information [8,27]. As concluded by Humbert & German [20], "there are tantalizing data that suggest various facets of oropharyngeal motor control and the interactions at various levels of the CNS during the normal swallow. However, the debate of whether the pharyngeal portion of the swallow is a reflex continues" ([20], p. 8). This debate centres on whether the motor sequence of the pharyngeal swallow remains constant, even in the presence of cortical modulation [9,15,26]. For example, the effortful swallow, whereby patients are instructed to 'swallow hard', has been shown to increase the overall amplitude of pharyngeal pressure [4,5,16,31,33]. Similarly, the manoeuvres such as the Mendelsohn, aiming to increase duration of upper oesophageal sphincter (UES) opening, and volitional laryngeal vestibule closure (vLVC), targeting increased duration of airway closure, have been shown to increase the overall duration of the pharyngeal swallow [10,17,25,32]. From these studies, it is accepted that we can volitionally modulate pressure and duration of contraction of the pharyngeal swallow, in its entirety [30]. But, it is still unclear if humans are capable of modulating select components of the pharyngeal swallow in isolation, such as the temporal sequence of pharyngeal closure.

Importantly, recent studies have added evidence regarding cortical contribution to the temporal sequencing of swallowing. German, Crompton, & Thexton [12] investigated the consistency of rhythmic muscle activation in decerebrate versus intact pig models using synchronized electromyography (EMG) and videofluoroscopy (VFSS). They reported that most of the temporal pharyngeal sequence from the reflexive swallow seen in the decerebrate animal group was also observed in the intact animal group, but the sequence of specific activity, such as geniohyoid activation, was substantially altered in the intact animal group [12]. It remains unclear if humans possess the capability to volitionally alter discrete elements of the overall motor plan of the pharyngeal phase of swallowing and, if so, to what extent.

A pathologic feature of dysphagia characterized by impairment of this basic temporal pharyngeal sequence has recently been reported in the literature [19]. The authors provide a description of a newly identified patient cohort (n = 16) with what was termed pharyngeal mis-sequencing, identified with pharyngeal manometry. Compared to a normative mean latency of 239 ms (95% CI, 215–263 ms) between peak pressure in the proximal-to-distal pharynx [24], this patient cohort presented with a latency of pharyngeal pressure generation in the distal pharynx of 15 ms (95% CI, −2–33 ms) following pressure generation in the proximal pharynx, in the presence of an overall increased duration of pharyngeal swallowing (620 ms; 95% CI, 469–770 ms) [19]. These patients did not demonstrate an overall change in pressure duration, rather a disproportionate and isolated change in the timing of peak pressure that was inversely correlated with timing of overall pressure. The presence of distorted latency of pharyngeal closure in this cohort led to substantial dysphagia in all patients, as evidence by inefficient and unsafe bolus transfer when swallowing, contributing to nasal redirection, aspiration, and, for some, an inability to safely tolerate oral intake.

Huckabee et al. [19] used pharyngeal manometry as a visual biofeedback modality in an intensive rehabilitation paradigm for this cohort. Once educated on the visual output generated from pharyngeal manometry, patients were instructed to volitionally increase the temporal separation between the proximal and distal pharyngeal pressure waveforms when swallowing. Following daily treatment, the mean latency between peak pressures at the proximal and distal pharynx increased from a pre-treatment average of 15 ms to a post-treatment mean of 137 ms (95% CI, 86–187 ms). It was conjectured that these patients were able to volitionally generate a cortical pharyngeal motor plan that either replaced or substantially modulated the medullary CPG motor plan, increasing temporal latency of proximal to distal pharyngeal closure when swallowing. The presence of such a capability was suggested by German et al. [12]. This aligns with patient reports of the need to maintain conscious awareness of swallowing to ensure generalization of gains following rehabilitation. However, this independent alteration in the latency of pharyngeal closure, as a representation of altered sequential muscle activation, challenges the commonly-held belief that the pharyngeal phase of swallowing is an involuntary reflexive sequence [9,29].

The aim of this exploratory study was to evaluate the capacity of healthy humans to volitionally alter the 'reflexive' components of the pharyngeal swallow. We sought to determine if healthy participants, upon completion of an intensive training protocol, could learn to modulate the temporal characteristics of peak pharyngeal pressure, specifically the latency of pressure generation between the proximal and distal pharynx using pharyngeal manometry as visual biofeedback. In essence, we evaluated the participants' capacity to replicate the initial presentation of the patient cohort with pharyngeal mis-sequencing [19]. We hypothesised that normal healthy adults would be able to adopt a motor plan which recruited pharyngeal pressure in both the proximal and distal pharynx, with a substantially reduced peak-to-peak separation between pharyngeal manometric sensors, following two weeks of daily biofeedback training. This would be accomplished without a simultaneous reduction in total swallowing duration, suggesting that the adaptation was one of volitional temporal shift of a specific component of swallowing rather than a more synergistic reduction in overall swallowing duration. This point is critical, as a proportionate reduction in swallowing duration would imply participants are merely swallowing at a faster rate, rather than disproportionately altering latency of pharyngeal closure in isolation. Successful modulation of the sequence of pharyngeal pressure generation by cortical control mechanisms would provide evidence to challenge the assumption that the sequence of pharyngeal pressure generation is a fixed and patterned reflexive response, unable to be cortically modulated. This would likely have important implications in the design of new approaches to dysphagia rehabilitation.

2. Materials and methods

2.1. Participants

Six healthy participants (3 males, 3 females), ranging in age from 19 to 44 years (mean = 29 years), participated in the study. No participant reported a history of dysphagia, neurological or muscular impairment, or use of any medications that might have affected swallowing. Ethical approval was obtained from the local institutional review board and

informed consent was obtained from all participants prior to commencement of data collection.

2.2. Equipment

A 100-cm-long catheter, 2.1 mm in diameter (Model CTS3 + EMG, Gaeltec, Hackensack, NJ, USA), was used for manometric data collection. As per standardized catheter recommendations from Salassa, DeVault, & McConnel [34], the catheter housed 3 solid-state, unidirectional, posteriorly-oriented sensors (2 × 5 mm) with 2-cm spacing between sensors 1 and 2, and 3 cm between sensors 2 and 3. Pressures were measured at the proximal pharynx, distal pharynx, and UES with sensors 1, 2 and 3 respectively. The catheter was connected to the Kay Elemetrics Digital Swallowing Workstation (Model 7120, Kay Pentax, Lincoln Park, NJ, USA), with digitized recording of pressure waveforms as a function of time displayed in real time in a −100 to 500 mm Hg display window on a computer screen, and digitally recorded for offline analysis.

2.3. Procedure

All participants were seen for intensive skill-based training daily for a period of two weeks (10 days), for a total of 10 one-hour sessions. This intensity was chosen to reflect the duration of intensive patient treatment used in local rehabilitation protocols [19]. Participants were seated upright in a comfortable chair. During each session, pharyngeal manometry was used as a visual biofeedback modality. At the beginning of the session, participants were shown images of manometric waveforms depicting normal pharyngeal pressure during swallowing, as shown in Fig. 1. Participants were educated on the goal of the training session, namely to reduce the separation between the peaks of the upper and lower pharyngeal sensors.

The lubricated intraluminal catheter was inserted into one naris, using routine clinical and research protocols [19]. A pull–through technique was performed in 5 mm increments. This was continued until correct catheter placement was confirmed through visualization of the typical 'M' wave at sensor 3 during swallowing, corresponding to the superior aspect of the high pressure zone of the UES [6]. Posterior orientation of the three sensors was confirmed by monitoring unidirectional markers on the catheter. The catheter was then secured to the nose with medical tape. At final placement, sensor 1 was located in the proximal pharynx (approximately at the level of the base of tongue), sensor 2 in the distal pharynx (approximately at the level of the laryngeal additus), and sensor 3 in the proximal aspect of the UES. Throughout data collection, evaluation of manometric waveforms by the researcher ensured correct placement was maintained. As modulation of UES function was not a focus of training, once placement was ensured, the waveform of sensor 3 was desaturated in colour to reduce visibility and to increase participant attention to the waveforms of sensors 1 and 2.

Each session consisted of collection of pre-training baseline swallows, to monitor whether training alters each participant's underlying swallowing motor plan, followed by three 15-min blocks of training utilizing the visual biofeedback, and ending with post-training swallows without visual biofeedback. To record baseline data, the computer monitor was turned away from the participants and they were asked to produce five typical (i.e., "normal") saliva swallows, without visualization of the waveform. Following the acquisition of baseline data, the participants were positioned to face the computer monitor. Using the real-time manometric data on the screen as visual biofeedback, the participants attempted to adapt swallowing behaviour in order to produce simultaneous pressure in sensors 1 and 2, performing dry swallows at a self-generated pace, approximately every 30–45 s. Directions included "try to make the red line come before the blue line" or "try to make your waveforms overlap." Sips of water were offered as needed to moisten the mouth. When the participants completed the three 15-min blocks of training, they were asked to perform their five 'best' mis-sequenced swallows without biofeedback (e.g., the computer monitor was turned away from the participants). Following these five swallows, the catheter was removed from the nasopharynx and the session ended. Participants had one session per day for 5 days per week over 2 weeks with the same protocol at each encounter.

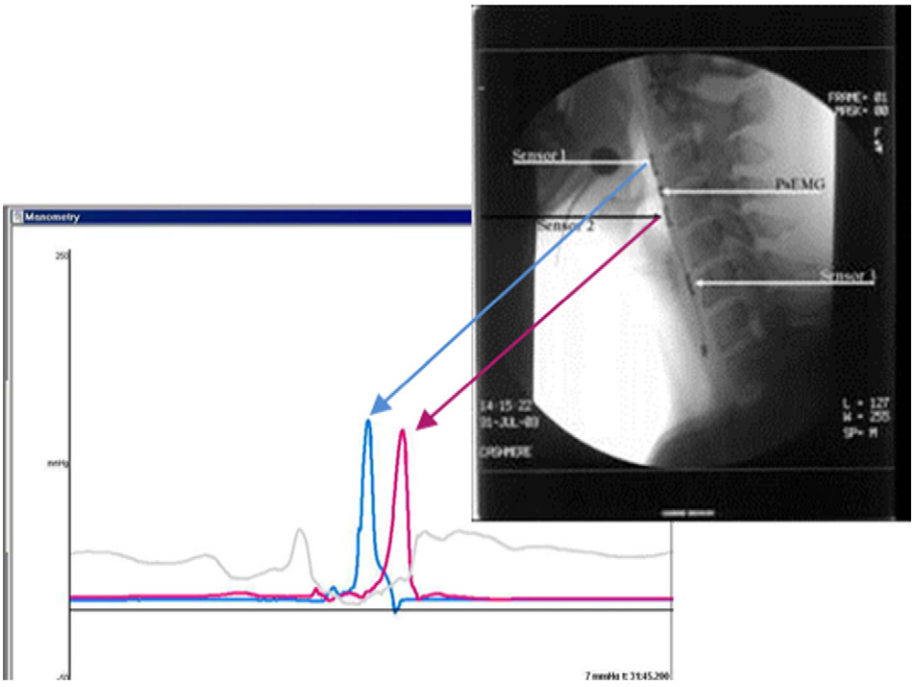

Fig. 1. Sample manometric waveforms used for participant training. The blue line indicates pressure generation in the proximal pharynx, and the red line indicates pressure generation in the distal pharynx. (See Huckabee et al. [19]; p. 156).

2.4. Data analysis

Five baseline swallows, a randomly selected 20% of swallows within each training session, and five post-training swallows *without* visual biofeedback were measured off-line for each subject using Kay Digital Swallowing Workstation software. Temporal values were measured with manually-placed, digital cursors for peak latencies of pharyngeal pressures generated at sensors 1 and 2 with peak-to-peak latency calculated as the difference between these two cursors. Total swallowing duration was measured from onset of pressure at sensor 1 to the offset of pressure at sensor 2. As onset measures were found to have poorer inter-rater reliability, swallowing onset and offset were measured at the point where the waveform crossed a horizontal cursor placed at 10% above the resting baseline, to remove bias in determine the onset of the waveforms. Amplitude data were measured using automated detection software to identify peak amplitude, and subsequently compared to peak-to-peak latency. Data were analysed using SPSS statistical software (IBM SPSS Statistics for Windows, Version 21.0, 2012, Armonk, NY: IBM Corp.).

Non-parametric statistical models were used due to the small sample size in the study and non-Gaussian distribution of the data (Shapiro–Wilk test, $p = 0.002$). Statistical analyses included descriptive statistics reporting medians and interquartile range (IQR) for all measures at baseline, session 5, and session 10. Friedman's tests, similar to the parametric repeated-measures analysis of variance, were used to detect differences in latency and total swallowing duration across participants for baseline, session 5, and session 10. Pair-wise comparisons were completed with a Wilcoxon signed-rank test. Pearson's product–moment correlation coefficient was used to analyse the relationship between change in peak-to-peak latency to change in average peak amplitude (across sensors 1 and 2) and swallowing duration, respectively. Inter- and intra-rater reliability (using a random 20% subset of the extracted randomized data) was analysed using two-way mixed intraclass correlation coefficient (ICC). The rater was a speech-language pathologist familiar with analysis of manometric waveforms, but naïve to the study aim and outcomes. Definitions were provided for the required latency and duration measurements. The rater was blinded to sessions and participants, and sessions were randomized during the reliability data collection procedure. As amplitude data were collected with automated detection software, reliability analysis was not undertaken for this measure.

3. Results

All participants completed the intensive training protocol without adverse event. Intra-rater reliability was high across measures ($\rho_c = 0.97$). Inter-rater reliability between two trained speech-language pathologists showed an excellent level of concordance for measures of peak-to-peak latency ($\rho_c = 0.94$), and total swallowing duration ($\rho_c = 0.89$).

3.1. Baseline swallowing

Baseline swallows collected at the beginning of each training session were consistent over the training period, with no significant differences between baseline measures at sessions 1, 5, and 10 for peak-to-peak latency ($p = 0.12$) and total swallowing duration ($p = 0.31$). Table 1 depicts baseline swallows across all training sessions.

3.2. Training sessions with biofeedback

Based on Friedman's test analyses, there was a significant reduction in peak-to-peak latency ($p = 0.002$), but no significant changes in overall total swallowing duration ($p = 0.41$) between training performance from session 1 baseline to session 5 training, and session 10 training. Session 1 pre-training and final session median and interquartile ranges are summarized in Table 2.

Pairwise analyses with Wilcoxon signed-rank tests revealed differences between peak-to-peak latencies at session 1 baseline and session 1 training ($p = 0.046$), session 1 baseline and session 5 training ($p = 0.028$), session 1 baseline and session 10 training ($p = 0.028$). There was a difference between session 1 training and session 5 training ($p = 0.028$), but no significant change between training sessions 5 and 10 ($p = 0.60$), as shown in Fig. 2. No significant differences were seen for total swallowing duration or amplitude between session 1 baseline and sessions 1, 5, or 10 training.

3.3. Post-training without biofeedback

Using a Friedman's test, results of the five post-training swallows at the end of each session, where participants were asked to volitionally modulate their swallow *without* biofeedback, were compared from session 1 baseline with post-training at sessions 1, 5, and 10, respectively. Participants demonstrated a reduction in peak-to-peak latency from a pre-training baseline median of 188 ms (IQR = 231) to 67 ms (IQR = 87; $p = 0.03$) at the end of session 10. In contrast to the findings from the training swallows, there was a difference between post-training swallows for total swallowing duration ($p = 0.03$), from an initial baseline median of 670 ms (IQR = 254) to a post-training median of 545 ms (IQR = 197).

Table 1
Median (IQR) baseline swallowing, as averaged between all sessions.

Measure	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5	Participant 6
Peak-to-peak latency	60 ms (56 ms)	84 ms (66 ms)	208 ms (79 ms)	103 ms (122 ms)	119 ms (154 ms)	239 ms (77 ms)
Swallowing duration	592 ms (70 ms)	610 ms (106 ms)	576 ms (194 ms)	555 ms (71 ms)	521 ms (120 ms)	700 ms (127 ms)
Onset duration	134 ms (48 ms)	76 ms (46 ms)	201 ms (56 ms)	102 ms (121 ms)	131 ms (58 ms)	305 ms (85 ms)

Table 2
Measures of pharyngeal swallowing (median and IQR) at session 1 pre-training and session 10 training.

Measure	Baseline	Session 5	% change from baseline	Session 10	% change from baseline
Peak-to-peak latency	188 ms (231 ms)	54 ms (97 ms)	71.3%	68 ms (92 ms)	63.8%
Swallowing duration	671 ms (254 ms)	623 ms (256 ms)	7.2%	595 ms (239 ms)	11.3%

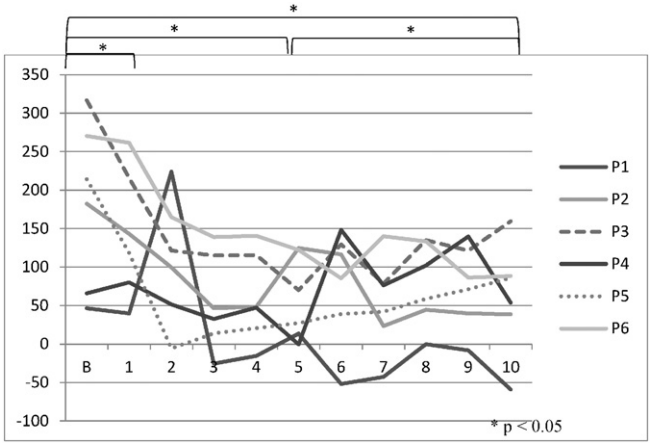

Fig. 2. Median peak-to-peak latencies for each participant.

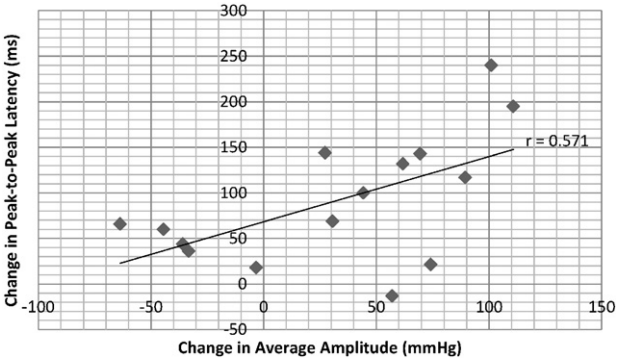

Fig. 3. Relationship between change in average amplitude and peak-to-peak latency during training (with biofeedback).

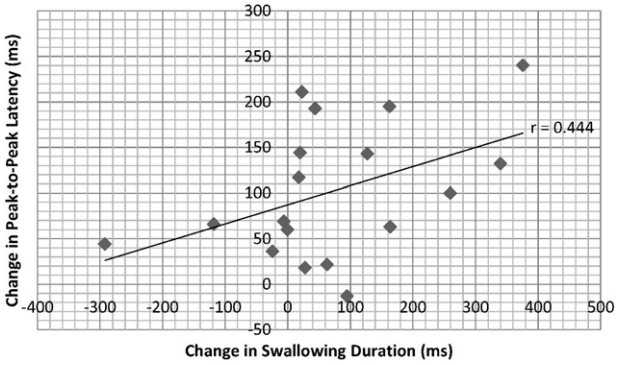

Fig. 4. Relationship between change in total swallowing duration and peak-to-peak latency during training (with biofeedback).

Pairwise analysis with Wilcoxon signed-rank test was also investigated between pre-training baselines versus post-training swallows without biofeedback at sessions 1, 5, and 10 (Table 3).

A comparison was completed with the Wilcoxon signed-rank test to determine the relationship between peak-to-peak latency of training swallows with biofeedback to post-training swallows without biofeedback in each session. There were no significant differences between peak-to-peak latency from session training with biofeedback to that session's post-training swallows without biofeedback. This confirms a consistent level of volitional control of modulation with and without visual biofeedback within sessions.

3.4. Correlation between swallowing features

Pearson's product–moment correlation coefficient was used to analyse the relationship between change in peak-to-peak latency to change in average peak amplitude during training to determine if there was a relationship between reduced latency of pharyngeal closure with increased amplitude of pharyngeal swallowing, as participants reported increased ease in altering timing of pharyngeal closure when 'swallowing hard'. Determinant of change was calculated by subtracting median values from baseline to training sessions 1, 5, and 10, respectively, within each subject for all participants. There was a linear correlation between peak amplitude and peak-to-peak latency ($r = 0.57$), as depicted in Fig. 3.

A similar analysis with Pearson's product–moment correlation coefficient was used to analyse the relationship between change in peak-to-peak latency and change in total swallowing duration during training to determine if there was a relationship between reduced latency of pharyngeal closure with a proportionate reduction in total swallowing duration. Determinant of change was calculated by subtracting median values from baseline to sessions 1, 5, and 10, respectively, within each subject for all participants, as used above. There was a linear correlation between peak amplitude and peak-to-peak latency ($r = 0.444$), as depicted in Fig. 4.

4. Discussion

This exploratory study is the first to evaluate the capacity of healthy adults to modulate the latency of pressure generation between the proximal and distal pharynx. Given intensive manometric biofeedback training, participants were able to substantially reduce the temporal separation between the peaks of the pharyngeal waveforms when volitionally swallowing, and maintain this gain immediately following the session without biofeedback. However, there was no further reduction seen during the second week of training. This indicates an effective limit in the newly acquired skill of altering pharyngeal sequence volitionally. Further, the median peak-to-peak latency achieved by the healthy participants (68 ms) was still above the 95% confidence interval of peak-to-peak latencies reported in the mis-sequencing patient group (15 ms, 95% CI, −2 to 33 ms) [19]. The limit in gains suggests that volitional modulation cannot alter the reflexive pharyngeal sequence to a pathologic level, as observed in the patient cohort.

The observation that participants had no significant change of pharyngeal timing in baseline 'normal' swallowing across the two-week

Table 3
Comparison of post-training swallows, without biofeedback, to initial baseline swallows.

	Peak-to-peak latency Median (IQR)	Comparison to baseline	Swallowing duration Median (IQR)	Comparison to baseline
Session 1 baseline	188 ms (231 ms)	–	670 ms (254 ms)	–
Session 1 post-training	132 ms (156 ms)	0.17	506 ms (835 ms)	0.03*
Session 5 post-training	30 ms (105 ms)	0.03*	650 ms (311 ms)	0.60
Session 10 post-training	67 ms (87 ms)	0.03*	545 ms (197 ms)	0.12

* Statistically significant finding.

training period may suggest that there was limited neural change, either at a cortical motor planning level overriding the brainstem response, or at the brainstem level of the medullary-mediated pharyngeal swallowing sequence, however this was not evaluated explicitly. Conversely, once biofeedback was provided after the baseline swallows, participants were able to volitionally alter swallowing peak latency, albeit not without considerable 'intra-session experimentation' in modulating the parameter of interest. Assessment with pre- and post-training fMRI could provide insights into neural change associated with this adapted pharyngeal response.

Huckabee et al. [19] speculated on the aetiology of the pathophysiologic feature of mis-sequencing and questioned whether this was a maladaptive response to impairment or reflected a feature of impairment from the brain injury itself. If this unique presentation of dysphagia was the result of a maladaptive mechanism, it would be logical that this impaired sequence could be normalized in patients given intensive rehabilitation with biofeedback [19]. However, being maladaptive would also imply that one has volitional control over the basic sequence of pharyngeal swallowing, challenging the commonly-held belief that the pharyngeal phase of swallowing is an involuntary reflexive sequence [9,29]. The healthy cohort in the present study provides evidence regarding the capability to alter the pharyngeal sequence with voluntary control. Interestingly, both the patient cohort described by Huckabee et al. [19] and healthy participants in the current study reported increased ease producing a mis-sequenced pattern when swallowing with effort. This finding is supported by a moderately strong relationship between change in peak-to-peak latency and change in peak amplitude ($r = 0.571$). Additionally, both cohorts similarly reported the need to maintain conscious attention during the biofeedback task to implement the desired pharyngeal response. As seen in a subgroup of patients in this study who did not benefit from treatment [19], three of the six subjects in the current study regressed by session 10, with peak-to-peak latency increasing from gains made at session 5. It is unclear if this regression reflects a loss of skill, variance due to small sample size or, rather, loss of attention and motivation during participation.

An important distinction should be made with regard to the proportion of change of latency of pharyngeal closure to total swallowing duration. Although participants were able to substantially reduce their peak-to-peak separation between pharyngeal manometric sensors without a simultaneous reduction in total swallowing duration during training swallows, there was a significant reduction in swallowing duration during the post-training swallows without biofeedback. This, in conjunction with the finding of a moderate relationship between change in peak-to-peak latency and change in swallowing duration ($r = 0.44$), would imply that participants are in large part merely modulating total swallowing duration to achieve the goal, rather than altering latency of pharyngeal closure in isolation. Although it is accepted we can volitionally modulate amplitude and duration of contraction of the pharyngeal swallow, in its entirety, it is still unclear if humans are capable of modulating the select components of the pharyngeal swallow in isolation, such as timing of pharyngeal closure. Further research is needed to clarify this point, as it is critical with regard to understanding the capability to fundamentally alter the pharyngeal motor plan, rather than optimizing the current plan (e.g., swallowing faster).

Biofeedback likely played a critical role in the ability to maximize cortical capacity to modulate aspects of pharyngeal swallowing, a reflexive function which is otherwise difficult to envisage. Other studies have evaluated the effect of biofeedback-enabled volitional modulation of presumed reflexive parameters of swallowing, such as UES opening and airway protection. Kahrilas, Logemann, Krugler, & Flanagan [23] used tactile biofeedback in conjunction with swallowing manoeuvres change to alter in UES opening in healthy participants ($n = 7$), as evaluated by manofluoroscopy. Similarly, Macrae et al. [25] trained healthy participants ($n = 16$) to perform a vLVC manoeuvre during swallowing either with or without biofeedback. Although these studies indicate UES opening, hyoid movement, and laryngeal vestibule closure are amenable to alteration by volitional control, of note, the basic sequence of pharyngeal swallowing was not altered. From studies of pig models, German et al. [12] concluded that humans may have only certain muscle groups or components of pharyngeal swallowing capable of cortical modulation, and, even then, only to a certain degree. This may have important implications when considering rehabilitation design and implementation. Understanding a healthy individual's capability to volitionally alter select components of pharyngeal swallowing is vital, as we can utilize this capability for cortical control during behavioural rehabilitation of impaired swallowing physiology [20]. However, it is critical to understand the impact that targeted rehabilitation has on the pharyngeal swallowing response overall. As the pharyngeal swallow is a highly orchestrated response, isolating targeted aspects can have unintended effects on the gestalt, as reported, for example, with increased nasal redirection as a result of an effortful swallowing paradigm [11].

Our study has limitations, which are important to acknowledge. This study is limited by small sample size, compounded by the use of non-parametric statistics, which may under-power findings and place the study at risk for Type II error. However, as several significant findings were identified, conservative sample sizes were deemed appropriate, especially due to the use of repeated, invasive and potentially uncomfortable procedures. Pharyngeal manometry does not directly allow visualization of swallowing physiology. Further research is indicated using manofluoroscopy to enable visual assessment of changes of biomechanics pre- and post-training to quantify how a change in pharyngeal timing affects swallowing parameters, if at all. Incorporation of videofluoroscopic evaluation can also provide insight on possible alteration of associated parameters during modulation of pharyngeal swallowing, such as pharyngeal shortening, and coordination with UES and laryngeal function. Further, as the manometric catheter is placed intraluminally, it is unknown whether the participants utilize any tactile feedback during the training task. Additionally, as pressure is a proxy measurement for timing of muscle contraction, a study utilizing pharyngeal electromyography (EMG) would be of value for further analysis of specific changes in temporal activation of muscle contraction itself. As this study did not include follow-up assessments after the two-week training period, ongoing data collection would be beneficial to determine the extent to which this new volitional control over pharyngeal swallowing is retained, without further biofeedback training or practice in healthy subjects.

Future studies will further explore the extent to which biofeedback training can be used by patients with dysphagia, to further investigate the role of volitional control on pharyngeal swallowing. Individualization of training targets could benefit future studies, as a participant's baseline peak-to-peak latency (e.g., long versus short) could impact the ability to modulate this characteristic of pharyngeal swallowing. This could be expanded in future studies by providing increasingly specific goal-oriented criteria to further delineate performance outcomes and effect of biofeedback. In contrast to healthy subjects, we hypothesise that dysphagic patients would continue to practice the adapted pharyngeal motor plan following the end of formal biofeedback training and, hence, will further increase, rather than lose, their newly found and highly beneficial skill.

5. Conclusions

This study revealed that intensive manometric biofeedback training enables healthy adults to substantially reduce the temporal separation between the peaks of the proximal and distal pharyngeal pressure waveforms when volitionally swallowing. However, this reduction was correlated with a contemporaneous change in total swallowing duration and amplitude, especially evident in the post-training condition. Further, the limit in gains suggests that cortical modulation cannot alter the reflexive pharyngeal sequence to a pathologic level. This ability

to gain volitional modulatory control over targeted aspects of the pharyngeal swallow may serve an important avenue for rehabilitative treatment of patients with pharyngeal mis-sequencing. Further research will determine how best to optimally gain volitional control of pharyngeal swallowing and, hence, design programmes for treatment of dysphagia.

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The authors declare that they have no conflict of interest.

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