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ORIGINAL ARTICLE

Swallow Event Sequencing: Comparing Healthy Older and Younger Adults

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Abstract
Previous research has established that a great deal of variation exists in the temporal sequence of swallowing events for healthy adults. Yet, the impact of aging on swallow event sequence is not well understood. Kendall et al. (Dysphagia 18(2):85–91, 2003) suggested there are 4 obligatory paired-event sequences in swallowing. We directly compared adherence to these sequences, as well as event latencies, and quantified the percentage of unique sequences in two samples of healthy adults: young (< 45) and old (> 65). The 8 swallowing events that contribute to the sequences were reliably identified from videofluoroscopy in a sample of 23 healthy seniors (10 male, mean age 74.7) and 20 healthy young adults (10 male, mean age 31.5) with no evidence of penetration–aspiration or post-swallow residue. Chi-square analyses compared the proportions of obligatory pairs and unique sequences by age group. Compared to the older subjects, younger subjects had significantly lower adherence to two obligatory sequences: Upper Esophageal Sphincter (UES) opening occurs before (or simultaneous with) the bolus arriving at the UES and UES maximum distention occurs before maximum pharyngeal constriction. The associated latencies were significantly different between age groups as well. Further, significantly fewer unique swallow sequences were observed in the older group (61%) compared with the young (82%) ($\chi^2 = 31.8$; $p < 0.001$). Our findings suggest that paired swallow event sequences may not be robust across the age continuum and that variation in swallow sequences appears to decrease with aging. These findings provide normative references for comparisons to older individuals with dysphagia.

Keywords Swallowing · Deglutition · Deglutition disorders · Dysphagia · Sequence · Temporal · Variation · Aging · Presbyphagia

Introduction

The safety and efficiency of swallowing is dependent upon the complex, rapid sequential contraction and relaxation of 30 pairs of bilaterally innervated muscles of the head and neck coordinated by five cranial and three peripheral nerves [1]. Establishing norms for not only the duration of events in the healthy swallow, but the sequence in which these events occur, allows investigators and clinicians to make comparisons between populations or to longitudinally track changes within an individual [2]. For example, one could examine whether airway closure is achieved prior to the point at which the bolus reaches the upper esophageal sphincter (UES). Failure to adhere to this sequence (laryngeal vestibule closure prior to arrival of the bolus at the UES) may result in compromised swallowing safety, given that the bolus would be adjacent to an open airway. In 2007, Mendell and Logemann conducted a review of studies examining temporal sequencing in the healthy swallow. They reported a great deal of variability in the use of measurement protocols. Importantly, they determined that several studies examined sequence in

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relation to a reference event—however, the reference event selected was not consistent across studies [2].

Kendall et al. [3] described an alternative approach to investigating swallow sequencing by quantifying the frequency with which 12-paired events occurred during the pharyngeal phase of a healthy swallow. The paired events were derived from the temporal events listed below (described in Kendall's original publication on page 87). For ease of interpretation, we have provided our own variable names in square brackets and these will be used in the remainder of this manuscript.

- *BP1*—Arrival of bolus head at UES [bolus at UES].
- *AEstart*—Beginning of superior arytenoid movement [laryngeal elevation].
- *AEclose*—First frame depicting laryngeal vestibule closure [laryngeal closure].
- *H2*—Maximum anterior–superior hyoid displacement [hyoid max].
- *Pop*—Beginning of UES opening [UES opening].
- *PESmax*—Point of maximum pharyngoesophageal segment distention [UES max].
- *HL*—Closest approximation of hyoid and larynx [hyolaryngeal approximation].
- *PAmax*—Point of maximum pharyngeal constriction [max PC].

In their sample of 60 healthy individuals (30 male) aged 18–62, they found a significant degree of variability in the order in which paired sequences occurred. This variability reportedly increased with smaller bolus sizes. However, four obligatory sequences (regardless of bolus volume) were identified:

1. *Laryngeal elevation* prior to *UES opening.*
2. *UES opening* prior to (or simultaneously with) *bolus at UES.*
3. *UES opening* prior to *hyolaryngeal approximation.*
4. *UES max* prior to *max PC.*

They also identified the most commonly occurring sequence of events as follows: *laryngeal closure* < *UES opening* ≤ *bolus at UES* < *hyoid max* < *UES max* < *hyolaryngeal approximation* < *max PC*. This sequence was found to occur 25% (45/180) of the time [3].

In 2014, Molfenter, Leigh, and Steele set out to replicate this study, in order to confirm the findings in a new sample restricted to young healthy adults (< 45 years old). Their study expanded on the original Kendall study given that, in addition to bolus size, barium viscosity and barium concentration were manipulated as well. Further, their study included three swallows per bolus condition in order to investigate sequence consistency across repeated trials. Molfenter and colleagues confirmed only two of Kendall et al.'s [3] obligatory sequences:

1. *Laryngeal elevation* prior to *UES opening.*
2. *UES opening* prior to *hyolaryngeal approximation.*

Additionally, Kendall et al.'s [3] most common sequence was only observed on 4/293 trials. In fact, the Molfenter study [4] identified 214 different event sequences, with only 3 sequences occurring 4 or more times. Neither bolus volume nor viscosity were found to influence the degree of variability in the sequence of swallow events. One exception was that smaller volumes resulted in increased variability for the *UES opening* prior to *hyolaryngeal approximation* sequence.

Ultimately, Molfenter and colleagues [4] concluded that a young healthy swallow is characterized by variability in the sequence of temporal events and hypothesized that this allows for flexibility in the face of unexpected demands. They identified variability in the swallow sequence of individuals with dysphagia as an area for future research. Specifically, they proposed that reduced variability in this population may impact their ability to adapt to different ways in which the bolus might travel through the pharynx [4].

It is widely accepted in the field that changes to swallowing occur as a normal part of the aging process. Specific age-related changes that may impact the temporal sequence of swallow events include increased oropharyngeal transit time [5], delayed initiation of the pharyngeal swallow [6–11], reduced tongue driving force and pharyngeal contractions [12, 13], reduced muscle strength and coordination [14–16], and reduced hyolaryngeal elevation [7].

Both the Kendall et al. [3] and Molfenter et al. [4] studies examined the variability of paired sequence occurrence in healthy adults under age 62. However, there is a significant gap in the literature regarding the impact of aging on the swallow sequence. Thus, this study specifically addresses the following questions:

(1) What proportion of healthy older individuals adheres to Kendall's original 4 obligatory sequences?
(2) Do obligatory sequences differ by age category?
(3) Do the latencies between event pairs in obligatory sequences differ by age category?
(4) What is the most common overall event sequence in a healthy older population?
(5) Does variation in swallow sequencing (represented by the number of unique overall sequences) differ by age category?

This work has important clinical ramifications. Presently, it is unknown how swallow sequence changes in the context of aging. Examining this is crucial, given that disordered swallowing typically occurs in the second half of life (secondary to stroke, cancer, degenerative disease etc.). Examining normal swallowing sequences in healthy aging adults will provide a normative reference for distinction between age-related changes to sequence variability, and changes that are seen in older dysphagic populations.

Materials and Methods

Participants

This IRB-approved study represents secondary analyses of two videofluoroscopic (VF) datasets: 20 healthy young adults (10 male, ages 22–45 with a mean age of 31.5) from the Molfenter and colleagues 2014 study and 23 healthy older adults (10 males and 13 females, ages 65–90, with a mean age of 74.7). Inclusion criteria for this analysis required the confirmation of safe and efficient swallowing on all boluses, using the Penetration–Aspiration Scale (PAS) [17] and Normalized Residue Ratio Scale (NRRS) [18]. Swallows with PAS scores of 1 or 2 were considered safe [19] and swallows with no significant residue (NRRSv < 0.082 and NRRSp < 0.067) were considered efficient [20]. Exclusionary criteria included a history of dysphagia, neurological insult/injury, and/or head and neck cancer or surgery. Swallow sequence data from the healthy young dataset have been previously published [4]; however, given that the healthy older dataset was collected with fewer swallow conditions, this analysis required that we identify and exclude swallow conditions (10 mL thin liquid at 20% w/v and the 5 mL thin liquid at 40% w/v) from the original healthy young dataset and recalculate proportions of events and sequences as required. Thus, it should be acknowledged that the data reported here for the healthy young dataset are different than those reported in the 2014 publication.

VF Procedure

For the healthy older dataset, VF was collected on a GE Advantix digital fluoroscope (GE Healthcare) at 30 pulses per second, and captured on a KayPENTAX digital swallowing workstation at 30 frames per second. Nine swallows per participant were included in this analysis: 3 × 5 mL thin liquid barium, 3 × 20 mL thin liquid barium, and 3 × 5 mL nectar thick barium. Barium stimuli were standard Varibar™ (Bracco Imaging); however the thin liquid barium was prepared to match the 20% w/v concentration of ‘ultra-thin’ stimuli used in the Molfenter [4] study. This preparation has been shown to improve detection of penetration–aspiration [21]. The order of stimuli was intentionally not randomized to minimize risk of potential aspiration of large volumes (5 mL prior to 20 mL) and to minimize contamination of post-swallow residue to later occurring swallows (which is more likely with nectar thick liquids). The procedures for data collection in the healthy young dataset are consistent with above and have been previously published [4].

Sequence and Latency Analysis

Individual swallows were spliced out of the full-length study for randomized analysis and identification of each of the following swallow events: *laryngeal elevation, laryngeal closure, UES opening, bolus at UES, hyoid max, hyolaryngeal approximation, UES max*, and *max PC*. These events were identified by the first author using frame-by-frame viewing of each swallow in *ImageJ* software (National Institutes of Health, Bethesda, MD) as per the guidelines laid out by Kendall et al. [3] using the operational definitions and modifications described by Molfenter and colleagues [4]. In the healthy older dataset, a total of 14 swallows were excluded from the analysis: seven due to inability to visualize the hyoid, two due to poor image quality, and five due to piecemeal deglutition. In the healthy young dataset, a total of 7 swallows were excluded due to piecemeal deglutition. As a result, 193 swallows from healthy older adults and 173 swallows from healthy young adults were included in the final analysis. Once the frame of each swallow event was identified, the order in which paired events occurred was determined. Data were then analyzed to quantify the proportion of swallows that obey Kendall’s four original obligatory sequences (Question 1), and compared across age groups (Question 2). Events occurring 97% of time or greater were considered obligatory [4]. For latency analysis, the frame on which the first event in a pair occurred was subtracted from the frame of the second event and converted to milliseconds by dividing by 30 (given the data were collected at 30 frames per second) and multiplying by 1000 (Question 3). Finally, the order of events was characterized for each swallow and tabulated (Questions 4 and 5).

Statistical Analysis

All data were analyzed using SPSS version 24. Questions 1 and 4 were answered using descriptive statistics. Chi-square statistics were used to compare proportions of obligatory sequencing by age (Question 2), as well as to compare the proportion of unique swallow sequences by age (Question 5). Repeated measures ANOVAs were used to compare the event latency by age category while controlling for repeated boluses per condition (Question 3). To control for the multiple comparisons problem, Bonferroni adjustments were applied and two-tailed p values < 0.0125 were considered statistically significant.

Results

Twenty percent of the data for healthy older adults, randomly sampled across participants and stimuli, was subject to inter- and intra-rater reliability ratings. Inter-rater reliability was conducted by a trained graduate student with experience in biomechanical analysis of swallowing. Reliability was examined in two ways. First, reliability of the adherence to Kendall's sequences [3] was examined using Cohen's Kappa scores [22]. These results are reported in Table 1. Next, the reliability of event latencies was examined using *laryngeal elevation* as a reference point. Latencies were calculated for all measured events, with the exception of *laryngeal elevation,* which by definition had a fixed latency. Reliability was established using two-way mixed intra-class correlation coefficients and the results are reported in Table 2. All latency measures achieved reliability scores of 'good–excellent' (> 0.75) [23]. Adequate reliability for the healthy young dataset was established and reported in the original Molfenter study [4].

Question 1. What proportion of healthy older individuals adheres to Kendall's original 4 obligatory sequences? Table 3 presents the frequencies with which Kendall's obligatory sequences occurred, broken down by bolus volume and viscosity. In accordance with Molfenter and colleagues' [4] definition, a sequence was said to be upheld in each cohort if it occurred at least 97% of the time, across conditions. The following sequences were found to hold true: *laryngeal elevation* prior to *UES opening, UES opening* prior to *hyolaryngeal approximation*, and *UES max* prior to *max PC*. The event pair *UES opening* before/with *bolus at UES* was not confirmed as obligatory. No clear patterns with respect to sequence differences by bolus volume or viscosity were noted. Additional figures that incorporate swallow trial, bolus volume, and bolus viscosity can be found in the Appendix.

Question 2. Do obligatory sequences differ by age category? Adherence to obligatory sequences was then compared between healthy young and healthy older datasets using Chi-square statistics (Table 4). Significant differences between age groups were found for two sequences: *UES opening* before/with *bolus at UES* ($\chi^2 = 193.154$, $p < 0.001$) and *UES max* before *max PC* ($\chi^2 = 35.137$, $p < 0.001$). For completeness, these comparisons were then re-tested in each bolus condition (5 mL thin, 20 mL thin, and 5 mL nectar), and confirmed to be significant for all comparisons.

Question 3. Do the latencies between event pairs in obligatory sequences differ by age category? Latencies (in milliseconds, ms) between the first and second event in an obligatory sequence are displayed in Table 5 below. Once again, significant differences were discovered between age groups for *UES opening* before/with *bolus at UES* and *UES max* before *max PC.* Younger subjects had longer (negative) latencies between *UES opening* and *bolus at UES* and older subjects had significantly prolonged (positive) latencies between *UES max* and *max PC*. Note that *UES opening* before/with *bolus at UES* had noticeably shorter latencies regardless of age compared to the other three event pairs.

Table 2 Intra- and inter-rater intra-class correlation coefficients (ICCs) and corresponding 95% confidence intervals (CI) for event latencies from *laryngeal elevation*

	Intra-rater			Inter-rater		
	ICC	95% CI		ICC	95% CI	
Bolus at UES	0.98	0.96	0.99	0.98	0.95	0.99
UES opening	0.98	0.96	0.99	0.98	0.95	0.99
UES max	0.97	0.95	0.99	0.91	0.83	0.95
Laryngeal closure	0.94	0.88	0.97	0.79	0.60	0.89
Hyolaryngeal max	0.93	0.87	0.96	0.81	0.65	0.90
Hyoid max	0.97	0.94	0.98	0.92	0.84	0.96
Max PC	0.96	0.93	0.98	0.88	0.77	0.94

Table 1 Intra- and Inter-rater agreement for adherence to obligatory sequences

Event order	Intra-rater			Inter-rater		
	Agreement (%)	Kappa	Interpretation	Agreement (%)	Kappa	Interpretation
Laryngeal elevation < UES opening	100.0	1.00	Almost perfect	97.5	0.66	Substantial
UES opening ≤ bolus at UES	94.9	0.72	Substantial	92.3	0.38	Fair
UES opening < hyolaryngeal max	100.0	1.00	Almost perfect	100.0	1.00	Almost perfect
UES max < max PC	100.0	1.00	Almost perfect	100.0	1.00	Almost perfect

Landis and Koch [22]: agreement levels 0–0.20 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.80 = substantial and 0.81–1 = almost perfect [23]

Table 3 Frequency (%) distribution of obligatory sequences across bolus viscosity and volume

Obligatory sequence	Adherence	5 mL thin (%)	20 mL thin (%)	5 mL nectar (%)	Overall (%)	*N*
Laryngeal elevation < UES opening	YES	100	95	100	98	190
	NO	0	5	0	2	3
UES opening ≤ bolus at UES	YES	81	92	85	86	166
	NO	19	8	15	14	27
UES opening < hyolaryngeal max	YES	98	98	97	98	189
	NO	2	2	3	2	4
UES max < max PC	YES	100	100	100	100	193
	NO	0	0	0	0	0

Table 4 Frequency distribution of obligatory sequences across age groups

Obligatory sequence	Adherence	Healthy young (%)	Healthy older (%)	χ^2	*p*
Laryngeal elevation < UES opening	YES	98	98	0.02	0.90
	NO	2	2		
UES opening ≤ bolus at UES	**YES**	**12**	**86**	**193.15**	**<0.001**
	NO	**88**	**14**		
UES opening < hyolaryngeal max	YES	98	98	0.02	0.88
	NO	2	2		
UES max < max PC	**YES**	**83**	**100**	**35.14**	**<0.001**
	NO	**17**	**0**		

Event pairs with a statistically significant difference in adherence between age groups have been indicated in bold

Table 5 Event latencies of obligatory sequences

Obligatory sequence	Healthy young			Healthy older			*F*	*p*
	Mean (ms)	Lower CI	Upper CI	Mean (ms)	Lower CI	Upper CI		
Laryngeal elevation < UES opening	234	199	268	222	189	254	0.26	0.613
UES opening ≤ bolus at UES	− 71	− 87	− 55	5	− 10	20	**50.19**	**<0.001**
UES opening < hyolaryngeal max	195	169	221	187	163	211	0.19	0.663
UES max < max PC	72	44	99	308	282	334	**158.4**	**<0.001**

Event pairs with a significant difference in latencies between age groups havebeen indicated in bold

Latencies calculated as Event 2–Event 1

Question 4. What is the most common overall event sequence in a healthy older population? Our analysis revealed marked variability in the sequence of swallow events. Kendall's most common event sequence (*Laryngeal closure < UES opening ≤ bolus at UES < hyoid max < UES max < hyolaryngeal approximation < max PC)* occurred on only two occasions (1%) in the healthy older dataset. Only five sequences were found to occur more than five times, accounting for between 2.5 and 6.2% of the sample. The most frequently occurring event sequence in this dataset was *UES opening/bolus at UES < laryngeal closure < UES max < hyolaryngeal approximation < hyoid max < max PC*, which was observed 12 times. This same pattern was found to occur only once in the healthy young dataset. The most frequently occurring sequence in that dataset was *bolus at UES < laryngeal closure < UES opening < UES max < hyolaryngeal approximation/max PC < hyoid max,* which occurred four times. This sequence was not seen in the healthy older dataset.

Question 5. Does variation in swallow sequencing differ by age category? Overall, 105 unique sequences were identified in 193 analyzed swallows (60.7%) from the healthy older dataset. This represents a significant decrease in variation when compared to the healthy young sample. There were 142 unique sequences identified in the relevant

Table 6 Percentage of unique sequences by swallow condition

Condition	Healthy young (%)	Healthy older (%)	$\chi2$	p
5 mL thin	90	86	0.48	0.489
5 mL nectar	92	77	**5.05**	**0.025**
20 mL thin	87	60	**10.76**	**0.001**

Conditions with a statistically significant difference in percentageof unique sequences are indicated in bold

Table 7 Percentage of unique sequences per participant by swallow condition

Condition	Healthy young (%)	Healthy older (%)
5 mL thin	100	98
5 mL nectar	98	96
20 mL thin	100	95
Total	98	90

swallows from the healthy young dataset out of 173 swallows (82.1%). This difference is highly significant ($\chi^2 = 31.8472$, $p < 0.0001$). Proportions of unique sequences were also tested by swallow condition, as detailed in Table 6 below. Significant reductions in variation in the older group were observed for the 5 mL nectar and 20 mL thin conditions but not the 5 mL thin condition. Finally, the proportion of unique swallows at the individual participant level was compared descriptively across age groups. Visual inspection of this data reveals a trend toward decreased variation at the participant level as well (Table 7).

Discussion

In this study, we examined four swallow event pairs that were previously identified by Kendall [3] as obligatory and later tested by Molfenter [4] in a healthy young dataset. The present study contributes novel data from healthy older adults (> 65 years old). The strength in this design is that the parameters, methods, and measures were nearly identical to those used in the healthy young dataset [4]. The exception is that more swallow conditions were collected in the healthy young dataset (3 × 10 mL and 3 × 5 mL at 40% w/v barium). These extraneous swallows were identified and excluded from the comparison analyses.

Two event pairs were found to be obligatory in both the healthy young and healthy older populations: *laryngeal elevation* before *UES opening*, and *UES opening* before *hyolaryngeal approximation.* Both of these results are expected, given the strong physiological ties between each event pair. Regarding *laryngeal elevation* before *UES opening,* this result is expected in healthy populations, given that (1) hyolaryngeal elevation is a key precipitating factor of UES opening [24], and (2) the *laryngeal elevation* event is a component of hyolaryngeal elevation. It remains to be seen whether this sequence remains obligatory in certain dysphagic populations. Regarding *UES opening* before *hyolaryngeal approximation,* in their definition of *hyolaryngeal max* Kendall and colleagues [3] specifically state that larynx-to-hyoid approximation occurs while the UES is open. This makes the sequence in question obligatory by definition, and of limited interest from a clinical standpoint.

One event pair, *UES max* prior to *max PC,* was confirmed in the healthy older sample, but not in the healthy young, with a statistically significant difference in adherence observed. A corresponding significant increase in event latency was observed in older versus younger datasets as well. This finding is consistent with literature on aging, which shows that pharyngeal contraction interval (onset-to-peak pharyngeal contraction) has been found to increase with age, while UES relaxation interval (onset-to-peak UES opening) has been found to decrease [25, 26]. Post hoc analysis of the current datasets revealed that maximum pharyngeal contraction was the last event to occur 99% of the time in healthy older adults vs. 36% in healthy young. This finding may have important implications related to post-swallow residue in dysphagic populations, particularly those with UES dysfunction.

Finally, *UES opening* before/with *bolus at UES,* was not confirmed in either population. According to the operational definition used in both the Molfenter [4] study and the current study, this sequence requires that UES opening occurs prior to or simultaneously with the arrival of the bolus at the base of the pyriform sinuses. Molfenter and colleagues noted that differences in the definition of *bolus at UES* may account for some of the inconsistency in the findings [4]. However, this explanation does not sufficiently explain the significant difference found between healthy young and healthy older populations. The directionality of this finding was particularly surprising (86% adherence in healthy older vs. 12% adherence in healthy young), given the reports that initiation of the pharyngeal swallow is delayed in healthy older adults, compared to healthy young [6–11, 27]. However, examination of the latencies for these paired events reveals less than a 80 ms difference between the two events. These findings are similar to reports by Logemann et al., who found a 30–40 ms difference between the point at which the bolus arrives at the level of the upper pyriforms and the point of UES opening, in both healthy young and healthy older populations [7, 25]. These findings confirm that bolus arrival at the pyriforms and UES opening are highly coupled events in healthy individuals, and lead us to question the clinical relevance of examining this sequence. Clinical utility is further brought into question when considering the fact that this sequence had the weakest reliability of the four, which may likely be attributed to the fact that these two events usually occur within one to two frames of each other. It remains to be seen whether this event pair, can meaningfully distinguish functional from impaired physiology in patients with dysphagia, especially in those patients with sensory deficits. Presumably, when an individual has reduced pharyngeal sensation, the bolus may pool at the base of the pyriforms for a prolonged period prior to *UES opening*.

While not one of our primary research questions, this dataset allowed us to look at trial-to-trial variability within a swallow condition by obligatory sequence. This is possible because each participant swallowed three-repeated boluses in each condition. These results are outlined in the Appendix for the healthy older dataset and appear in the original publication for the healthy young dataset. Interestingly, for *UES opening* before/with *Bolus at UES*, the least amount of variation was seen for the 20 mL condition. Similarly, the greatest decrease in overall sequence variability was noted in the 20 mL condition. This finding corroborates both Molfenter and Kendall's findings that smaller bolus volumes appear to have greater variation. It is possible that this decrease in variation is explained by the fact that the 20 mL condition most closely approximates natural drinking behaviors [28]. While there appear to be differences by bolus trial number within bolus conditions for the *UES opening* before/with *Bolus at UES* sequence, no clear patterns of order affect can be elucidated across conditions. No notable differences were observed for the remaining three sequences, given the high degree of adherence across bolus conditions.

In regards to overall sequence, while a most common sequence was identified in the healthy older population, this sequence did not occur frequently enough to be deemed clinically relevant. Of interest, is the finding that significantly less variation occurred in the healthy older population, when compared to healthy young–a finding which is consistent with previous research [7]. This appears to hold true across swallow conditions at both the individual and group level. A possible explanation for this lies in increased pharyngeal transit times (PTT) observed in aging. While a recent systematic review examining swallow timing in aging notes that findings of increased PTT with aging are sparse, a lack of direct comparisons between age groups within reviewed studies was also acknowledged [27]. A direct comparison between datasets used in this study reveals a trend towards increased PTT in aging, for both the 5 and 20 mL thin conditions. In the healthy young dataset, average PTT was reported to be 471 ms and 528 ms for 5 and 20 mL thin liquid boluses, respectively [29]. In the corresponding healthy older adults, we found that the average PTT was 614 ms for 5 mL thin liquid boluses and 699 ms for 20 mL thin liquid boluses. The shorter PTT in younger individuals requires that swallowing events happen more rapidly, with shorter latencies, thus increasing the likelihood that the order of events will vary.

This study is not without limitations. First, this study is limited by the narrow range of volumes, viscosities, and textures tested. While notable variation was not observed between 5 mL thin and 5 mL nectar boluses, it is plausible that greater variation may have been seen, given a wider range of stimuli. It remains to be seen whether sequence variation differs between liquid and solid stimuli. An additional limitation is that while the sample was sex-balanced, sex differences were not directly tested. Finally, this study could be strengthened with the identification and inclusion of bolus past mandible (BPM). The BPM event is incorporated into variables that quantify the onset of pharyngeal swallowing. Given that pharyngeal swallow trigger is known to be delayed in aging populations [6–11], this may have served as an interesting point for comparison.

Further testing of certain event pairs in dysphagic populations, specifically *UES opening* before/with *bolus at UES* and *UES max* prior to *max PC,* appears to be warranted. It is the opinion of these authors that future research examining event pairs should be expanded to pairs of events that have direct implications on the safety and efficiency of the swallow. One such example is *laryngeal elevation* before/with *BPM.* This sequence would capture the beginning of airway closure in relation to the point that the bolus enters the pharynx. Changes in this sequence may directly impact swallow safety. Another event pair warranting exploration is *laryngeal vestibule opening* from *UES opening* and/or *UES max* as this too may yield important information regarding swallow safety. Lastly, it is the opinion of these authors that future research should include a 'naturally-occurring sip' condition, as this study has provided anecdotal evidence that in healthy populations, variability may be induced by our manipulation of bolus volume.

Conclusions

Our findings suggest that paired swallow event sequences may not be robust across the age continuum and that variation in overall swallow sequences appears to decrease with aging. Findings regarding obligatory sequence adherence and, perhaps more importantly, latency, provide normative references that may be used as a basis of comparison for individuals with dysphagia. This study has proposed relevant sequences for future studies, added support to a body of evidence that indicates increased pharyngeal transit times with aging, and perhaps most importantly, provided preliminary evidence for the impact of bolus volume on swallow variability.

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Compliance with Ethical Standards

Conflict of interest This work was presented as a poster presentation at the 2018 Dysphagia Research Society Conference (DRS). No other conflicts of interest to disclose.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Appendix

See Figs. 1, 2, 3, and 4.

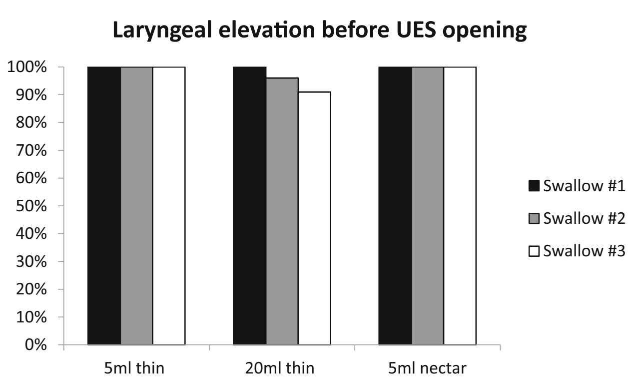

Fig. 1 Percentage of swallows in the healthy older dataset adhering to obligatory sequence of *laryngeal elevation* before *UES opening* by trial, bolus size, and viscosity

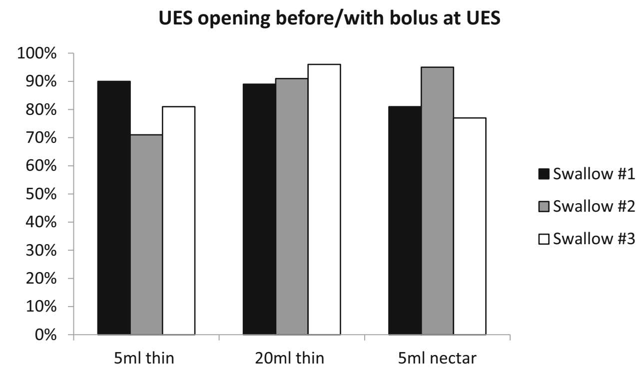

Fig. 2 Percentage of swallows in the healthy older dataset adhering to obligatory sequence of *UES opening* before or with *bolus at UES* by trial, bolus size, and viscosity

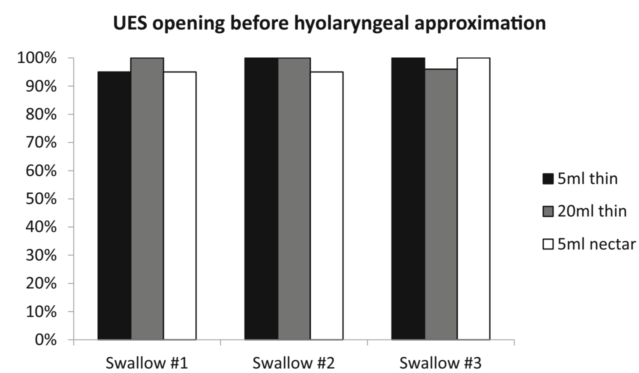

Fig. 3 Percentage of swallows in the healthy older dataset adhering to obligatory sequence of UES opening before *hyolaryngeal approximation* by trial, bolus size, and viscosity

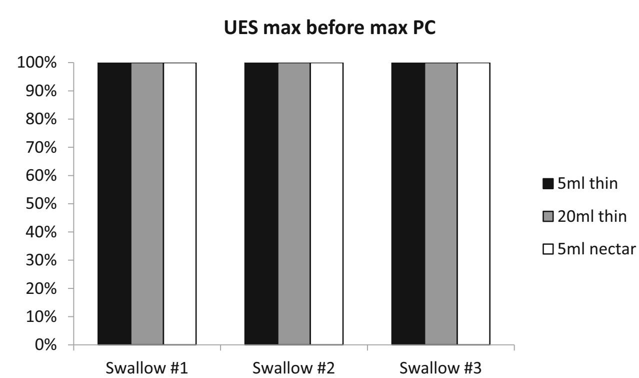

Fig. 4 Percentage of swallows in the healthy older dataset adhering to obligatory sequence of *UES max* before *Max PC* by trial, bolus size, and viscosity

References

1. Shaw SM, Martino R. The normal swallow: muscular and neurophysiological control. Otolaryngol Clin North Am. 2013;46(6):937–56.
2. Mendell DA, Logemann JA. Temporal sequence of swallow events during the oropharyngeal swallow. J Speech Lang Hear Res. 2007;50(5):1256–71.

3. Kendall KA, Leonard RJ, McKenzie SW. Sequence variability during hypopharyngeal bolus transit. Dysphagia. 2003;18(2):85–91.
4. Molfenter SM, Leigh C, Steele CM. Event sequence variability in healthy swallowing: building on previous findings. Dysphagia. 2014;29(2):234–42.
5. Yokoyama M, Mitomi N, Tetsuka K, Tayama N, Niimi S. Role of laryngeal movement and effect of aging on swallowing pressure in the pharynx and upper esophageal sphincter. The Laryngoscope. 2000;110(3):434–9.
6. Tracy JF, Logemann JA, Kahrilas PJ, Jacob P, Kobara M, Krugler C. Preliminary observations on the effects of age on oropharyngeal deglutition. Dysphagia. 1989;4(2):90–4.
7. Logemann JA, Pauloski BR, Rademaker AW, Colangelo LA, Kahrilas PJ, Smith CH. Temporal and biomechanical characteristics of oropharyngeal swallow in younger and older men. J Speech Lang Hear Res. 2000;43(5):1264–74.
8. Yoshikawa M, Yoshida M, Nagasaki T, Tanimoto K, Tsuga K, Akagawa Y, et al. Aspects of swallowing in healthy dentate elderly persons older than 80 years. J Gerontol Ser A: Biol Sci Med Sci. 2005;60(4):506–9.
9. Martin-Harris B, Brodsky MB, Michel Y, Lee F-S, Walters B. Delayed initiation of the pharyngeal swallow: normal variability in adult swallows. J Speech Lang Hear Res. 2007;50(3):585–94.
10. Molfenter SM, Steele CM. Temporal variability in the deglutition literature. Dysphagia. 2012;27(2):162–77.
11. Robbins J, Hamilton JW, Lof GL, Kempster GB. Oropharyngeal swallowing in normal adults of different ages. Gastroenterology. 1992;103(3):823–9.
12. Dejaeger E, Pelemans W, Ponette E, Joosten E. Mechanisms involved in postdeglutition retention in the elderly. Dysphagia. 1997;12(2):63–7.
13. Kendall KA, Leonard RJ. Pharyngeal constriction in elderly dysphagic patients compared with young and elderly nondysphagic controls. Dysphagia. 2001;16(4):272–8.
14. Aminpour S, Leonard R, Fuller SC, Belafsky PC. Pharyngeal wall differences between normal younger and older adults. ENT: Ear Nose Throat J. 2011;90(4):E1–5.
15. Molfenter SM, Amin M, Branski R, Brumm J, Hagiwara M, Roof S, et al. Age-related changes in pharyngeal lumen size: a retrospective MRI analysis. Dysphagia. 2015;30(3):321.
16. Evans WJ. What is sarcopenia? J Gerontol Ser A: Biol Sci Med Sci. 1995;50(Special_Issue):5–8.
17. Rosenbek JC, Robbins JA, Roecker EB, Coyle JL, Wood JL. A penetration-aspiration scale. Dysphagia. 1996;11(2):93–8.
18. Pearson WG, Molfenter SM, Smith ZM, Steele CM. Image-based measurement of post-swallow residue: the normalized residue ratio scale. Dysphagia. 2013;28(2):167–77.
19. Allen JE, White CJ, Leonard RJ, Belafsky PC. Prevalence of penetration and aspiration on videofluoroscopy in normal individuals without dysphagia. Otolaryngol Head Neck Surg. 2010;142(2):208–13.
20. Steele C, Chak V, Dhindsa A, Nagy A, Peladeau-Pigeon M, Tapson M, Torreiter S, Wolkin T, Waito A. How much residue is too much residue? Oral presentation at 5th ESSD Congress in Barcelona, Spain, October 2015. Abstr Publ Dysphagia. 2016;31:259–60.
21. Fink TA, Ross JB. Are we testing a true thin liquid? Dysphagia. 2009;24(3):285–9.
22. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159–74.
23. Enderlein G, Fleiss J. The design and analysis of clinical experiments. New York: Wiley; 1986.
24. Cook IJ, Dodds WJ, Dantas R, Massey B, Kern MK, Lang IM, et al. Opening mechanisms of the human upper esophageal sphincter. Am J Physiol Gastrointest Liver Physiol. 1989;257(5):G748–59.
25. Logemann JA, Pauloski BR, Rademaker AW, Kahrilas PJ. Oropharyngeal swallow in younger and older women: videofluoroscopic analysis. J Speech Lang Hear Res. 2002;45(3):434–45.
26. van Herwaarden MA, Katz PO, Gideon RM, Barrett J, Castell JA, Achem S, et al. Are manometric parameters of the upper esophageal sphincter and pharynx affected by age and gender? Dysphagia. 2003;18(3):211–7.
27. Namasivayam-MacDonald AM, Barbon CA, Steele CM. A review of swallow timing in the elderly. Physiol Behav. 2017. https://doi.org/10.1016/j.physbeh.2017.10.023.
28. Bennett JW, Van Lieshout PH, Pelletier CA, Steele CM. Sip-sizing behaviors in natural drinking conditions compared to instructed experimental conditions. Dysphagia. 2009;24(2):152–8.
29. Molfenter SM, Steele CM. Variation in temporal measures of swallowing: sex and volume effects. Dysphagia. 2013;28(2):226–33.

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