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Original Research

Assessing the Effect of Fatigue on Swallowing Function in Adults with Acute Stroke. A Pilot Study

Hope E. Baylow, DA

Peninsula Hospital Center, Department of Speech-Language Pathology and Audiology, Far Rockaway, NY
The University of Scranton, Department of Health and Human Performance, Scranton, PA

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Abstract *Objective:* To determine if fatigue systematically effects the timing of swallowing events and to discuss underlying causes of fatigue other than peripheral neuromuscular fatigue.
Design: Pre-post within-subject repeated-measures design.
Setting: General acute care hospital and designated stroke center.
Participants: Thirteen patients (10 males and 3 females) aged 52-80 years (mean 64.84±9.58 y) with acute stroke and clinically suspected dysphagia.
Interventions: Under videofluoroscopy, each participant swallowed a pre- and post-study 1-mL liquid barium bolus and, in an attempt to fatigue the system, 30-45 additional bolus trials of varying amounts (ie, 5 mL, 10 mL, and bite-sized) and consistencies (ie, International Dysphagia Diet Standardisation Initiative Level 0-7).
Main Outcome Measures: Six temporal sequences (ie, oral, pharyngeal, and pharyngeal delay transit times and durations of laryngeal vestibule closure, cricopharyngeal opening, and laryngeal elevation) for 1-mL liquid boluses were measured pre- and postvideofluoroscopic swallowing study and compared.
Results: Findings indicated that only 2 of the 6 temporal factors yielded significant differences pre- to post fatigue. The postvideofluoroscopic 1-mL liquid swallow took longer than the pre-videofluoroscopic 1-mL liquid swallow in terms of pharyngeal transit ($_{1,11}$=5.362, P=.046) and pharyngeal delay time ($F_{1,11}$=5.228, P=.048).
Conclusions: These findings indicate that peripheral neuromuscular fatigue is unlikely to be the primary cause of the observed changes, as only 2 of the 6 temporal measures—pharyngeal transit time and pharyngeal delay time—were affected. In cases of peripheral neuromuscular fatigue, one would expect increases across all 6 timing measures due to the integrated nature of the swallowing process. Instead, the results suggest that the inconsistencies may stem from a delayed excitatory response of neurons or a delay in synaptic transmission within the nucleus tractus solitarius, potentially associated with stroke. This delay likely contributes to the prolongation of both pharyngeal

List of abbreviations: CPG, central pattern generator; IDDSI, International Dysphagia Diet Standardisation Initiative; NTS, nucleus tractus solatarius; VFSS, videofluorographic swallowing study.

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transit and pharyngeal delay times. Thus, a model focused solely on peripheral neuromuscular fatigue does not fully account for the findings, highlighting the importance of considering central neural mechanisms in the clinical evaluation of swallowing disorders.

Neuromuscular fatigue is a reduction in the contraction capacity required to generate maximal muscle force, which can affect the physiological functioning of the swallowing mechanism.[1-3] It can be further classified as either central or peripheral and prolonged or short-term, each of which impacts swallowing performance differently. Central neuromuscular fatigue, associated with the central nervous system, limits neural transmission to muscles, often acting as a protective mechanism to prevent overuse.[2] Peripheral neuromuscular fatigue, on the other hand, occurs at the muscle level due to energy depletion, affecting muscle strength, endurance, and coordination.[1,3-6] The primary difference between prolonged and short-term muscle fatigue is its duration, underlying causes, and recovery time.

Prolonged fatigue lasts for hours, days, or even longer, persisting well beyond the period of activity.[3,7,8] It can be caused by more complex factors, including central nervous system involvement (central fatigue), where the brain and spinal cord reduce the ability to activate the muscles effectively, or a combination of central and peripheral factors,[2] neuromuscular dysfunction, or the result of repeated strenuous exercise that induces long-lasting muscle damage, inflammation, or glycogen depletion.[1,7] Prolonged fatigue may take longer to recover from, ranging from days to weeks, depending on the extent of muscle damage, glycogen depletion, or nervous system recovery,[1] and may lead to more lasting changes in muscle function, such as delayed-onset muscle soreness or sustained weakness, often requiring more extended recovery periods.[9]

Short-term fatigue occurs after a brief period of intense or repetitive muscle use and typically resolves within minutes to a few hours.[2] It may result from temporary metabolic changes,[3] such as the accumulation of lactic acid, depletion of energy stores (adenosine triphosphate), or changes in ion balance (eg, calcium or potassium) during intense activity.[10] Short-term fatigue is often more related to peripheral fatigue and the peripheral neuromuscular system due to the limitations of the muscle level itself (eg, reduced availability of adenosine triphosphate or build-up of metabolic byproducts),[4] resolves quickly once the immediate metabolic or biochemical imbalances are corrected, often within a few minutes to hours of rest,[4] and tends to be more reversible with quick rest and hydration.[10]

In neurotypical individuals, the oral phase of swallowing is a voluntary process initiated by descending cortical signals and sensory feedback. In contrast, the pharyngeal and esophageal phases are reflexive and follow an irreversible sequence once triggered by the oral phase. These reflexive phases are governed by distinct neural groups in the medulla, with the dorsal swallowing group and ventral swallowing group playing essential roles in their coordination.[11-13] Understanding peripheral neuromuscular fatigue is key to designing effective therapeutic swallowing exercise plans. Because different types of fatigue—central, peripheral, prolonged, and short-term—can affect performance, distinguishing between them is important for treating individuals with poststroke dysphagia. Recognizing how each type of fatigue impacts neuropathological conditions enables practitioners to develop more effective rehabilitation strategies, potentially improving therapeutic outcomes and allowing for more accurate assessments of treatment efficacy in stroke-related swallowing disorders.

One way to study neuromuscular fatigue in swallowing is by using the videofluoroscopic swallowing study (VFSS). Duration measures from the VFSS can capture swallowing fatigue by evaluating the timing and efficiency of swallowing across repeated trials.[14] Swallowing fatigue may manifest as a decline in the performance of key swallowing functions over time, which the VFSS can objectively quantify by observing changes in various measures related to the timing and coordination of the swallow.

This pilot study aimed to examine the effect of a fatigue condition on swallowing by assessing various swallowing metrics obtained through the VFSS and to differentiate the contributions of central and peripheral fatigue to these swallowing metrics. This study aimed to determine whether systematically fatiguing the swallowing mechanism in adults with acute stroke would lead to an increase in oral and pharyngeal swallowing times and to explore potential causes beyond peripheral neuromuscular fatigue. It was hypothesized that inducing fatigue would lead to longer durations for all the temporal measures being evaluated.

The investigation aimed to answer 2 research questions:

(1) Does oral transit time, pharyngeal transit time, pharyngeal delay time, duration of laryngeal vestibule closure, duration of cricopharyngeal opening, and duration of laryngeal elevation increase with use in adults with acute stroke when an effort is made to “fatigue” the swallowing mechanism?
(2) If there is a systematic effect of use on swallow function, specifically a change in the duration of oral and pharyngeal swallowing in adults with acute stroke when an effort is made to “fatigue” the swallowing mechanism, is it due to peripheral neuromuscular fatigue?

Methods

Study population

VFSS data for 13 adult participants diagnosed with acute stroke were analyzed for temporal swallow measures. The author’s institutional review board approved the study design, study methods, and informed consent process before

Table 1 Site of lesion - frequency and percentage distribution

(1) Variable (X)	(2) Frequency (f)	(3) Percentage (%)
Ischemic; cortical; right	5	38.5
Ischemic; cortical; left	0	0
Ischemic; subcortical; right	1	7.7
Ischemic; subcortical; left	1	7.7
Ischemic; brainstem; right	1	7.7
Ischemic; brainstem; left	1	7.7
Hemorrhagic; cortical; right	2	15.3
Hemorrhagic; cortical; left	0	0
Hemorrhagic; cortical; bilateral	1	7.7
Hemorrhagic; subcortical; right	0	0
Hemorrhagic; subcortical; left	0	0
Hemorrhagic; subcortical; bilateral	1	7.7
Hemorrhagic; brainstem; right	0	0
Hemorrhagic; brainstem; left	0	0
Hemorrhagic; brainstem; bilateral	0	0
	n=13	100.0%

the study's enrollment. Written consent was obtained from each participant or, in the case of confusion or dysphasia, from the next of kin or advocate. The participant's physician also cosigned the informed consent statement, acknowledging that the patient had agreed to participate in the research project. There was no compensation for participant involvement because the VFSS was only performed as a component of the patient's standard medical care.

The participants were aged 52-80 years (mean 64.84± 9.58 y). There were 10 males and 3 females. All participants underwent a clinical swallowing screening using the Northwestern Dysphagia Patient Check Sheet[15] and VFSS within 1-35 days (mean 9.9 d) after stroke onset. Each participant hospitalized for stroke was identified using a designated stroke center care map (ie, a standardized protocol used by certified stroke centers to provide optimal care for patients experiencing a stroke) and had a modified Rankin scale score of 4. Physician interpretation of brain imaging (computed tomography and/or magnetic resonance imaging) confirmed that all 13 participants had suffered an acute stroke. The frequency and percentage distribution of the site of lesion are listed in table 1.

Participant selection procedures

Data collection used purposive sampling to identify patients within the population who met specific criteria. The criteria for selection included: diagnosis of acute stroke provided by a medical doctor (classified as ischemic or hemorrhagic; cortical, subcortical, or brainstem; and right, left, or bilateral) and confirmation of no previous stroke, referral by a physician for the assessment of possible dysphagia, an adequate level of consciousness to participate in a swallowing evaluation, medical stability, and no history of progressive neurologic disease, head and neck cancer, dysphagia before hospitalization, or the presence of a tracheostomy, nasogastric, or gastrostomy tube.

Clinical swallowing screening

The Northwestern Dysphagia Patient Check Sheet[15] was used to screen each participant's swallowing function within 3 days of receiving a physician's request for the evaluation of possible oropharyngeal dysphagia. This 28-item screening procedure introduces minimal risk to patients because various consistency amounts are nominal.[15] The screening tool comprised 28 patient variables that are commonly considered when determining if a patient presents with dysphagia and the need for instrumental assessment.

Videofluoroscopic swallowing study

The VFSS is designed to study the function of the oral cavity, pharynx, and cervical esophagus and complements the clinical swallowing screening. Within 24 hours of the clinical swallowing screening, a VFSS was performed by the speech-language pathologist and radiologist, who were blinded to the outcome of the clinical swallowing screening. Each VFSS included a pre- and poststudy 1-mL liquid barium swallow.[16] Bolus volume selection was guided by procedures described by Logemann[17] and Daggett et al.[16] To "fatigue" the swallowing mechanism, each participant's VFSS included two 1-, 3-, 5-, and 10-mL swallows of thin barium liquid (International Dysphagia Diet Standardisation Initiative [IDDSI] Level 0), mildly thick liquid (IDDSI Level 2), and moderately thick liquid (IDDSI Level 3), two 5- and 10-mL amounts of extremely thick (IDDSI Level 4), and 2-4 bite-size amounts of solid (IDDSI 6). Relative radiation levels were monitored for each patient and remained within the adult effective dose estimate range of 1-10 mSv.

Participants were seated upright in a Hausted video imaging chair with their head in a neutral position. The study was completed using the lateral plane, viewing the oral cavity (anterior to the lips), the pharynx (the posterior pharyngeal wall posteriorly and the velum superiorly), and the cervical esophagus (inferiorly to the seventh cervical vertebra). The

samples were recorded using a Siemens Panteskop 35 fluoroscopy machine[a] and a Panasonic DMR-ES40V VHS/DVD recorder[b] (VHS Recording SQPB VHS Hi-Fi), which permitted forward and reverse viewing at variable speeds and still-frame and frame-by-frame evaluation. A low-viscosity barium suspension was used using a 2:1 dilution of E-Z-HD (120 w/v, E-Z-EM Inc)[c], with the viscosity of water for each 1-mL pre- and post-VFSS liquid swallow that was recorded.

Procedures for temporal measurements

The temporal sequences of oropharyngeal swallowing events were measured using slow motion, frame-by-frame analysis at 30 frames per second. Each pre- and post-VFSS 1-mL liquid barium swallow was measured, following the procedures reported by Kleinjan and Logemann,[14] for the following points of incidence: (1) oral transit time: the time interval in seconds from the first posterior movement of the bolus head in the oral cavity to the point when the head of the bolus reaches the inferior edge of the ramus of the mandible; (2) pharyngeal transit time: the time interval in seconds from the moment the bolus head passes the inferior edge of the ramus of the mandible to the closing of the cricopharyngeal sphincter after passage of the bolus tail; (3) pharyngeal delay time: the time from the moment the bolus head reaches the inferior edge of the ramus of the mandible until the moment the larynx begins to elevate in relation to the swallow; (4) duration of laryngeal vestibule closure: the length of time in seconds that the laryngeal entrance between the arytenoid cartilage and base of epiglottis is closed in the lateral plane during the swallow; (5) duration of cricopharyngeal opening: the length of time in seconds from when the cricopharyngeal region opens to allow passage of the bolus into the esophagus to the time when the region closed after passage of the bolus tail; and (6) duration of laryngeal elevation: the length of time in seconds between the beginning of laryngeal ascent to the time it returns to resting position during a swallow. To account for premature spillage from the oral cavity into the pharyngeal space (eg, valleculae, pyriform sinuses) that occurs in patients poststroke,[18] the onset of oral transit was represented by the first purposeful posterior movement of the bolus head (ie, the tongue propelling the bolus posteriorly).[19]

Primary outcome

The primary outcome was that delayed temporal events in pharyngeal transit and pharyngeal delay time exist in adults with acute stroke when an effort is made to fatigue the swallowing mechanism.

Variables

Age, time after stroke onset, and possible relationships between the clinical swallowing screening characteristics (eg, oral motor function and language/cognitive skills) and the temporal variables were analyzed as covariates but had no significant effect.

Statistical analysis

Descriptive statistics

The temporal measures for each specified marker were recorded and subjected to statistical analysis. To assess whether there was a significant difference within the 1-mL trials over time, the analysis focused on the effect of the independent variable, time of swallow (1-mL pre- and 1-mL post-VFSS), on the dependent variables, which included oral transit time, pharyngeal transit time, pharyngeal delay time, and the duration of laryngeal vestibule closure, cricopharyngeal opening, and laryngeal elevation. The following descriptive statistics are reported: mean, median, and standard deviations for pre- and post-VFSS 1-mL duration measures. Descriptive statistics for the swallowing measures are presented in table 2.

Exploratory inferential analyses

Inferential statistics are typically recommended with larger samples (eg, N=30 or more) because they can identify potential patterns or trends in the data. These trends might not reach full statistical significance with small sample sizes, but they can still provide preliminary evidence that justifies further research with larger samples. In this way, small-sample studies can help to generate hypotheses for future research, especially when exploring new or underresearched areas. Further, inferential statistics allow for the calculation of effect sizes. The data for adults with acute stroke were analyzed using a repeated-measures analysis of variance design, considering the appropriate degrees of freedom for the within-subjects factor. *T*-tests were used for follow-up analyses, and Cohen's d was used to measure effect sizes. The significance level for all statistical tests was set at an alpha level (α) of 0.05. Given the preliminary nature of the study, a Bonferroni correction was not applied to the multiple comparisons to avoid reducing statistical power. Analyses were performed using SPSS, version 22 (2013)[d] and JASP 0.18.3[e].

Table 2 Descriptive statistics, *P* values, and effect sizes for pre- and post-VFSS 1-mL duration measures

	Pre Median (s)	Post Median (s)	Pre Mean (s)	Pre SD (s)	Post Mean (s)	Post SD (s)	*P* value for *t* test	Effect Size
Oral transit time	0.670	0.545	0.605	0.407	0.521	0.333	.081	0.622
Pharyngeal transit time	1.030	3.760	1.678	1.509	6.230	7.210	.028	−0.690
Pharyngeal delay time	0.630	3.300	1.082	1.400	5.412	7.107	.034	−0.665
Duration of laryngeal vestibule closure	0.500	0.470	0.505	0.141	0.492	0.100	.790	0.076
Duration of cricopharyngeal opening	0.470	0.530	0.479	0.122	0.532	0.146	.096	−0.500
Duration of laryngeal elevation	0.930	1.100	1.045	0.318	1.058	0.286	.827	−0.062

Results

Descriptive statistics

Four timing measures showed similar pre- to posttest timing. For oral transit time, the mean time decreased from pretest (0.605±0.407 s) to posttest (0.521±0.333 s). Two patients showed increased oral transit time, while all others experienced a decrease for pre- to post-1-mL swallows. Six patients showed decreased timing pre- to posttest for the duration of laryngeal vestibule closure, while the other 7 patients showed slightly increased timing pre- to posttest. Changes from pretest to posttest ranged from 0.36 seconds faster to 0.44 seconds slower, pretest to posttest. For cricopharyngeal opening, 4 patients showed decreased timing pre- to posttest, while the other 9 patients showed slightly increased timing pre- to posttest. Changes from pretest to posttest ranged from 0.14 seconds faster to 0.24 seconds slower, pretest to posttest. Finally, for laryngeal elevation, changes from pretest to posttest ranged from 0.44 seconds faster to 0.37 seconds slower, with 6 patients showing decreased timing while the other 7 patients showed slightly increased timing pre- to posttest.

The remaining 2 measures showed a trend of increased durations for pre-and post-VFSS 1-mL duration. For pharyngeal transit time, 1 patient experienced no change, 1 patient experienced a slight decrease in duration, and 11 patients experienced an increased pharyngeal transit time pretest to posttest (mean 1.678±1.509 s vs 6.230±7.210 s, respectively). Changes in pharyngeal transit time ranged from 0.13 seconds faster pretest to posttest to 21 seconds slower pretest to posttest. Similarly, there was an increase in pharyngeal delay time, pretest to posttest (mean 1.082±1.400 s vs 5.412±7.107 s). Two patients experienced no change, pretest to posttest, while 11 patients experienced an increased pharyngeal delay time, pretest to posttest, ranging from 0 seconds to 20.83 seconds.

Exploratory inferential analyses

There was no significant change in the duration of oral transit time ($F_{1,11}$=3.868, P=.081) between the pre- and post-1-mL swallows and no significant effect on duration of laryngeal vestibule closure ($F_{1,11}$ =0.009, P=.925), duration of cricopharyngeal opening ($F_{1,11}$=0.983, P=.347), and duration of laryngeal elevation ($F_{1,11}$=0.503, P=.496). However, both pharyngeal factors yielded significant differences, with the post-1-mL swallow taking longer than the pre-1-mL swallow in terms of pharyngeal transit time ($F_{1,11}$=5.362, P=.046) and pharyngeal delay time ($F_{1,11}$=5.228, P=.048) (fig 1).

The mean oral transit time decreased from pretest (0.605±0.407 s) to posttest (0.521±0.333 s), though this change was not statistically significant, (t_9=1.967, P=.081, d=0.622). The pharyngeal transit time showed a significant increase from pretest (mean 1.678±1.509 s) to posttest (mean 6.230±7.210 s, t_{12}=−2.489, P=.028, d=−0.690). Similarly, the pharyngeal delay time increased significantly from pretest (mean 1.082±1.400 s) to posttest (mean 5.412±7.107 s, t_{12}=−2.399, P=.034, d=−0.665).

For the duration of laryngeal vestibule closure, there was a slight decrease from pretest (mean 0.505±0.141 s) to posttest (mean 0.492±0.100 s), but this was not statistically significant (t_{12}=0.273, P=.790, d=0.076). The duration of cricopharyngeal opening showed an increase from pretest (mean 0.479±0.122 s) to posttest (mean 0.532±0.146 s), but this difference was not significant (t_{12}=−1.804, P=.096,

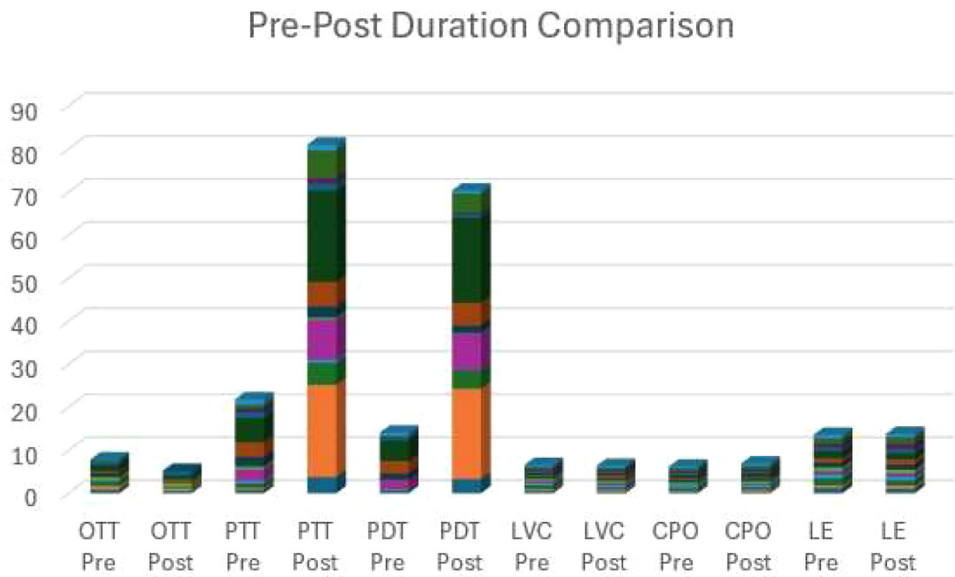

Fig 1 Pre to Post duration comparison. This bar graph illustrates the comparison of temporal duration measures before (Pre) and after (Post) a VFSS (videofluoroscopic swallowing study) across different phases of the swallowing process for 13 participants. The specific measures compared include oral transit time (OTT), pharyngeal transit time (PTT), pharyngeal delay time (PDT), duration of laryngeal vestibule closure (LVC), duration of cricopharyngeal opening (CPO), and duration of laryngeal elevation (LE). The height of the bars indicates the duration in seconds for each measure, with the Pre and Post values presented side by side for direct comparison. The data suggest notable differences in PTT and PDT, where posttest durations are significantly longer than pretest durations.

d=−0.500). Finally, the duration of laryngeal elevation showed minimal change between pretest (mean 1.045± 0.318 s) and posttest (mean 1.058±0.286 s), with no significant difference found (t_{12}=−0.223, P=.827, d=−0.062).

Discussion

Understanding and differentiating between various types of fatigue—central, peripheral, prolonged, and short-term—appears to be an important consideration in individuals with poststroke dysphagia. The ability to distinguish between these fatigue types and their unique impacts on neuropathological conditions may enhance the development of more targeted and effective rehabilitative strategies. Such differentiation could optimize therapeutic outcomes and provide more accurate assessments of treatment efficacy in patients with stroke-related swallowing disorders.

This study provides preliminary evidence of increased pharyngeal transit and pharyngeal delay time with 1-mL trial swallows of liquid barium in adults with acute stroke when an effort is made to "fatigue" the swallowing mechanism. However, no evidence of increased oral transit time or duration of laryngeal vestibule closure, cricopharyngeal opening, or laryngeal elevation under the same conditions was found. Although the sample size was small, the pilot data suggest a neurophysiological control of oral and pharyngeal swallowing, consisting of biomechanical actions and reflexive events occurring in succession, with the reflexive events operating independently.

It was hypothesized that inducing fatigue would result in longer durations across all 6 temporal measures of swallowing; however, the results did not support this hypothesis. Contrary to expectations, not all 6 measures showed a consistent increase in duration after the fatigue condition. In this study, pharyngeal transit times for pre-VFSS 1-mL liquid bolus swallows ranged from 0.43 to 5.73 seconds, and post-VFSS times ranged from 0.50-21.43 seconds. Pre-VFSS, 9 of 13 participants had transit times within the normal range (1.11±0.40 s),[20] but post-VFSS, only 2 of 13 maintained normalcy. The mean pre-VFSS transit time was 1.678 seconds, increasing significantly to 6.230 seconds post-VFSS (table 3).

Pharyngeal delay times ranged from 0.03-4.77 seconds pre-VFSS and from 0.03-21.0 seconds post-VFSS. Pre-VFSS, 4 of 13 participants had delay times within the normal range (0.06±0.07 s),[21] but post-VFSS, only 2 of 13 remained within normal limits. The mean delay time increased significantly from 1.082 seconds pre-VFSS to 5.412 seconds post-VFSS (table 3).

Previous research has shown that pharyngeal transit times are not affected by bolus volume, sex, or aging.[22-25] Our findings show that 69% of participants had typical transit times pre-VFSS, compared to only 15% post-VFSS. This suggests that central nervous system factors or fatigue may independently influence pharyngeal transit time. Similarly, while 38% of participants had normal pharyngeal delay times pre-VFSS, only 15% did post-VFSS, pointing to potential effects of central or peripheral fatigue.

Interestingly, oral transit time and duration of laryngeal vestibule closure, cricopharyngeal opening, and laryngeal elevation showed no significant changes pre- and postfatigue, contrary to the hypothesis that fatigue would uniformly affect all measures. These findings suggest that these

Table 3 Pharyngeal levels for 13 participants

Participant	Age/Sex	Stroke	Days Post Onset for Clinical Swallow Screening	Northwestern Dysphagia Patient Check Sheet Total Score	Pharyngeal Transit Time		Pharyngeal Delay Time	
					Pre-VFSS 1-mL Swallow (s)	Post-VFSS 1-mL Swallow (s)	Pre-VFSS 1-mL Swallow (s)	Post-VFSS 1-mL Swallow (s)
1	54M	RIS	3	9	0.83	**3.76**	**0.86**	**3.3**
2	63M	RHC	4	18	0.43	**21.43**	**0.17**	**21.0**
3	52M	BHC	17	15	1.03	**5.17**	0.10	**4.3**
4	65M	RIC	6	11	0.57	0.57	0.03	0.03
5	66M	LIS	15	13	**2.7**	**9.4**	**1.9**	**8.43**
6	76F	BHS	14	11	0.63	0.50	0.06	0.17
7	75F	RIC	3	9	**2.27**	**2.53**	**1.5**	**1.7**
8	71M	RIC	3	13	**3.37**	**5.73**	**2.87**	**5.33**
9	71F	RIB	1	11	**5.73**	**21.27**	**4.77**	**19.83**
10	80M	RIC	16	12	1.23	**1.66**	**0.63**	**0.70**
11	53M	RIC	5	11	0.97	1.2	**0.30**	**0.43**
12	64M	RHC	35	13	0.83	**6.47**	0.10	**4.43**
13	53M	LIB	6	13	1.23	1.30	**0.77**	**0.70**

NOTE. Pharyngeal transit time (1.11±0.40 s).[12] Pharyngeal delay time (0.06±0.07 s).[13] A score of >8 of 28 observations using the Northwestern Dysphagia Patient Check Sheet predicts a pharyngeal delay with 70% accuracy (sensitivity of 69% and specificity of 71%).[10]
Abbreviations: BHC, bilateral hemorrhagic cortical; BHS, bilateral hemorrhagic subcortical; F, female; LIB, left ischemic brainstem; LIS, left ischemic subcortical; M, male; RHC, right hemorrhagic cortical; RIB, right ischemic brainstem; RIC, right ischemic cortical; RIS, right ischemic subcortical; VFSS, video fluoroscopic swallowing study.

components of the swallow may be more resistant to fatigue than the other pharyngeal factors (ie, pharyngeal transit time and pharyngeal delay time). Longer pharyngeal transit and delay times may reflect disrupted neurophysiological control of swallowing or an autonomic response. Fatigue, as induced in this study, did not uniformly affect the swallowing mechanism. The lack of significant changes in some measures indicates that the impact of fatigue may be more complex than initially thought, involving factors beyond peripheral neuromuscular fatigue, such as central neural mechanisms or compensatory strategies employed by the swallowing system. These findings highlight the need for further investigation, especially given the small sample size and potential impact of bolus volume and viscosities on how different types of fatigue influence the coordination and timing of the swallowing process.

Neurophysiological mechanisms underlying swallowing

The results of this study highlight the complexity of the neural control involved in swallowing, which integrates both central and peripheral inputs with direct linkage in the medulla. Swallowing relies on a bilateral sensorimotor process orchestrated by central pattern generators (CPGs) such as the nucleus tractus solitarius (NTS) and nucleus ambiguus, which process afferent inputs from cranial nerves IX and X as well as higher central neural structures.[12] This integration generates a pattern of excitation and inhibition, coordinating the activation of motoneurons controlling the muscles involved in swallowing.[11-13,26,27]

In neurotypical individuals, the oral phase of swallowing is a volitional event[11] initiated through descending cortical inputs and sensory feedback. However, consistent changes in oral transit time were not observed, suggesting that the volitional aspect of swallowing may not be as susceptible to fatigue-induced changes as the reflexive phases. By contrast, the pharyngeal and esophageal phases are reflexive and occur in irreversible succession once triggered by the oral phase.[12,13,28] Anatomically, these phases are governed by separate neuron groups in the medulla, with the dorsal swallowing group and ventral swallowing group playing key roles.[11-13] The findings of prolonged pharyngeal transit and pharyngeal delay time under fatigue conditions suggest that these reflexive events may be more vulnerable to the effect of central or peripheral fatigue.

Additionally, sensory fibers of the superior laryngeal nerve and their synaptic pathways in the medulla contribute to the modulation of motor output, particularly in the ventral medullary region, which controls laryngeal muscle reflexes.[26,27] The lack of changes in laryngeal vestibule closure and cricopharyngeal opening duration in the results suggests that the reflexive control of these muscles may remain intact even under fatigue conditions, potentially reflecting the resilience of ventral synaptic pathways.

Although not directly measured in this study, the esophageal phase of swallowing relies on a balance of excitatory and inhibitory signals controlling smooth and striated muscle contractions.[29] Previous research suggests esophageal motoneurons are inhibited during the oropharyngeal phase, with contractions initiated by afferent inputs once the bolus enters the esophagus.[30] While the present study focused on pharyngeal measures, the potential effect of fatigue on esophageal function, mainly due to the vagal motor nucleus's role in autonomic regulation, remains an area for future investigation.

These findings underscore the role of central neuronal mechanisms in maintaining swallowing function under fatigue. The lack of uniform alterations across all temporal measures suggests that different components of the swallowing mechanism exhibit varying levels of susceptibility to fatigue. Future studies should investigate how these central and peripheral inputs interact across all phases of swallowing, particularly under conditions of neuromuscular fatigue, to improve therapeutic interventions for patients with pathophysiological conditions such as stroke-induced dysphagia.

Clinical importance

This study provides key insights into the impact of fatigue on swallowing in adults with acute stroke, showing that pharyngeal transit time and pharyngeal delay time significantly increase after fatigue. According to the CPG hypothesis, once a swallow is initiated, a sequence of excitatory and inhibitory signals in the premotor circuitry and motoneurons guides the process, which involves the pharyngeal and esophageal phases of swallowing.[11,31,32] This sequence is thought to be centrally regulated,[11] with minimal reliance on peripheral sensory input, meaning that swallowing is largely controlled by central nervous system activity. Key regions such as the NTS and nucleus ambiguus are responsible for this centrally patterned motor activity, especially in the pharyngeal and esophageal phases of swallowing.[13,26,27]

The present study's analysis shows statistically significant differences in only 2 temporal measures—pharyngeal transit time and pharyngeal delay time—among the 6 metrics evaluated. While this finding should be interpreted with caution due to the small sample size, the effect sizes for these differences were medium to large. This suggests that the difference between the pre-and poststudy is substantial, and the fatigue observed is statistically significant and likely important in real-world applications. Additionally, it should be noted that the criopharyngeal opening effect size was moderate, so this result could be more impactful with a larger sample size. These results were surprising, as based on Jean's work,[11] an all-or-nothing effect should have been observed due to the volitional initiation of the oral phase and subsequent pharyngeal phase triggered by the CPGs. This discrepancy suggests that additional factors may have influenced the swallowing function in acute stroke patients. These factors may include the initiation of a modulated effect or the employment of a safety process to protect the patient from aspiration or other risks.

These data support the idea that bidirectional communication between the pharynx and cortical regions is essential for ensuring the proper timing and magnitude of the swallowing response.[33] This study highlights the role of central nervous system fatigue and CPG dysfunction as potential contributors to swallowing difficulties and poor oral intake in patients with acute stroke rather than purely peripheral neuromuscular fatigue, a finding also reported by Cook et al[34] in the healthy aged individual and Bisch et al[35] in

patients with stroke. Although the sample is small, it does lend preliminary support to heterarchical control in which there is interdependence between the reflexive components of swallowing and the function of the CPGs responsible for the synergistic and stereotyped swallowing pattern. The data suggest that traditional behavioral rehabilitation may benefit from adding neuromodulatory interventions to address central and peripheral fatigue. Further investigations are warranted to explore these mechanisms in larger populations and to refine therapeutic interventions for post-stroke dysphagia, aiming to optimize both the efficiency and safety of the swallowing process.

Study limitations

Some limitations of the current pilot study include sampling a small, heterogeneous group of participants, the variable number of boluses administered, and the variation in bolus volume and viscosities. Neuromuscular fatigue was inferred based on changes in durational measures pre- and post-VFSS. Moreover, the study did not include any objective measure of fatigue, patient inquiries about fatigue-related symptoms, or a stroke severity rating. Additional studies with larger patient populations are necessary to determine if the duration changes identified in the pharyngeal transit time and pharyngeal delay time findings are associated with central nervous system fatigue, as suggested by these data.

Conclusions

The VFSS has been instrumental in helping researchers and clinicians identify the temporal characteristics of the oral and pharyngeal phases of swallowing. It has provided valuable insights into the systematic changes in swallowing patterns observed in both healthy aging populations and individuals who have experienced acute strokes. Clinicians rely on the objective data from the VFSS to create tailored management and treatment plans. Thus, a deep understanding of the neurologic aspects of fatigue, including the roles of the central swallowing network, CPGs, and the biomechanical properties of both neurotypical and disordered swallowing, is critical for optimizing patient care.

The distinction between peripheral neuromuscular fatigue, defined as the reduction in muscle force after sustained or repeated use, and central nervous system fatigue, which may arise from impaired neural transmission, is essential in understanding swallowing dynamics. In this study, the muscles involved in the swallowing sequences were consistent across different conditions. Given that neurologic and biomechanical mechanisms govern swallowing, one would expect significant differences across all events or none at all. However, the inconsistent results suggest a possible delayed excitatory response of the NTS neurons or a delay in synaptic transmission within the NTS, potentially due to stroke. This may have contributed to the findings of pharyngeal transit time and pharyngeal delay time. As a result, a model based solely on peripheral neuromuscular fatigue does not appear to fully explain the observed outcomes, highlighting the importance of considering central neural mechanisms in the clinical evaluation of swallowing disorders.

Suppliers

a. Siemens Panteskop 35 fluoroscopy machine, Siemens Healthcare, a division of Siemens AG. b. Panasonic DMR-ES40V VHS/DVD recorder, Panasonic Corporation. c. E-Z-HD, E-Z-EM Inc. d. SPSS, version 22; IBM SPSS. e. JASP, version 0.18.3; JASP Team, University of Amsterdam.

Corresponding author

Hope E. Baylow, D.A., The University of Scranton, Edward Leahy Hall, 824, Scranton, PA 18510. *E-mail address:* hope.baylow@scranton.edu.

Disclosures

The author declares there are no conflicts of interest.

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