

Review Article

## The Role of Fatigue in the Aging Swallow: A Review

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### Abstract

Fatigue is a term commonly used to describe patient performance and/or subjective experience in the evaluation and management of swallowing disorders (known as *dysphagia*). There is an association between fatigue and aging, as well as fatigue and many dysphagia-causing diseases/disorders. Therefore, speech-language pathologists (SLPs) are justifiably aware of and concerned about the potential impact of fatigue on swallowing performance and mealtime behavior. However, there is minimal agreement on and understanding of what constitutes swallowing-related fatigue, how it is identified and measured, who is at risk, and its impact on swallowing function, overall health, and quality of life. The purpose of this review is to discuss the role of fatigue in swallowing and eating behavior in the context of aging, and how fatigue may be measured and managed clinically. We review the concept of fatigue and its clinical implications for swallowing function and mealtime behavior through the dichotomous framework of self-perceived fatigue versus measurable fatigability. Quantitative



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fatigability and patient-reported fatigue are discussed. We conclude with implications for future research.

### **Keywords**

Dysphagia; aging; swallowing-related fatigue; fatigability

## **1. Introduction**

### **1.1 Fatigue in Aging**

Fatigue is frequently reported by older adults and is a common reason for seeking medical care [1, 2]. Fatigue in older adults can be extremely debilitating as it may interfere with activities of daily living (e.g. eating, dressing, hygiene [3] and quality of life [4, 5], and is associated with higher risk for disability onset [6]. Associations between fatigue and many medical conditions have been well established, including cancer [7], stroke [8], multiple sclerosis [9], chronic obstructive pulmonary disease [10], and osteoarthritis [11], yet fatigue may also present in the absence of any definitive cause [12]. The prevalence of fatigue is difficult to estimate, but has been reported to affect between 20 and 55% of community-dwelling older adults [13], and as many as 98% of individuals living in residential care facilities [14]. Together with unintentional weight loss, weakness, slow walking speed, and low physical activity, fatigue is a key clinical indicator of frailty [15]. Importantly, a diagnosis of frailty is most prevalent among older adults [16], and is associated with increased risk for adverse health outcomes, mortality [15] and dysphagia, (i.e. swallowing impairment) [17, 18], which is the focus of this review.

### **1.2 Introduction to Swallowing-Related Fatigue**

Consuming a meal is generally considered an enjoyable, even relaxing, and often social experience for healthy, non-dysphagic individuals. Yet, meal consumption involves a host of complex motor, cognitive, homeostatic, psychosocial, and cultural factors that must interact to result in a safe, efficient, and pleasurable experience [19-22]. Impairments in any part of this process can lead to reduced mealtime safety [23], health (e.g. malnutrition and/or dehydration) [24, 25] and quality of life [26, 27]. Impairments may also impact an individual's eating behavior, which collectively refers to food choices and motives, feeding practices, dieting, and eating related problems such as eating and feeding disorders [28]. Swallowing is central to the act of meal consumption, and encompasses the entire process from oral preparation of the food or liquid (e.g. chewing), to transporting it from the oral cavity, through the pharynx, past a closed larynx, and into the esophagus [29]. Continual swallowing over the course of a meal can be considered an endurance task, given that, in addition to sustained attention, it requires sustained, repetitive and continuous submaximal performance (i.e. requiring only a fraction of total force capacity) of a wide array of muscles [30]. The muscles involved in safe and efficient swallowing include lingual, facial, palatal, pharyngeal, laryngeal, and respiratory muscles (see Kent [31] for a detailed review of craniofacial and laryngeal muscle structure and function). These muscles include both Type I, slow twitch,

fatigue resistant and Type II, fast twitch, muscle fiber types, given their complex and important role for breathing, swallowing, and communicating [32-35].

Because swallowing and eating require endurance, impaired endurance, or easy fatigability, has the potential to negatively affect this vital human behavior. An individual's ability to safely and efficiently consume a complete meal could potentially be impacted by either declines in swallowing performance increasing risk for aspiration (i.e. airway invasion) and/or the need to stop prematurely due to fatigue, thus increasing the risk for malnutrition and impaired quality of life. These considerable health risks may be amplified in older adults and dysphagic populations in whom fatigue is common, including those with frailty, peripheral neurological disease (e.g. Myasthenia Gravis), central neurological disease (e.g. stroke, Parkinson's Disease), and cognitive impairment (e.g. Alzheimer's Disease, dementia). Individuals with psychological disorders (e.g. depression) are also at risk for meal-related fatigue due to changes in motivation, mood, and appetite [36, 37].

Yet, the relevance of fatigue during swallowing may be underappreciated due to the nature of how dysphagia is evaluated and diagnosed. Clinical and instrumental evaluations assess a brief "snapshot" of swallowing performance during a few sips and bites of liquids and foods. Whether this snapshot is representative of swallowing performance over the course of a full meal is a frequent source of discussion and speculation among dysphagia researchers and speech-language pathologists (SLPs), and represents a limitation in dysphagia evaluation and diagnosis [38]. Thus, while considerable attention has been given to researching the impact of force and pressure generation of lingual [e.g. 39-41] and pharyngeal [e.g. 39, 42, 43] swallowing musculature, as well as skill-based physiological parameters [e.g. 44, 45] on dysphagia and dysphagia rehabilitation, the potential role of fatigue in dysphagia is largely unknown and understudied.

Fundamental questions that need to be answered include how to define swallowing-related fatigue, and how fatigue affects swallowing physiology and function. Further, it is important to understand whether swallowing-related fatigue can be quantified to determine thresholds for risk, and the nature of the relationship between the patient-reported fatigue and measurable fatigability during swallowing are gaps in current knowledge.

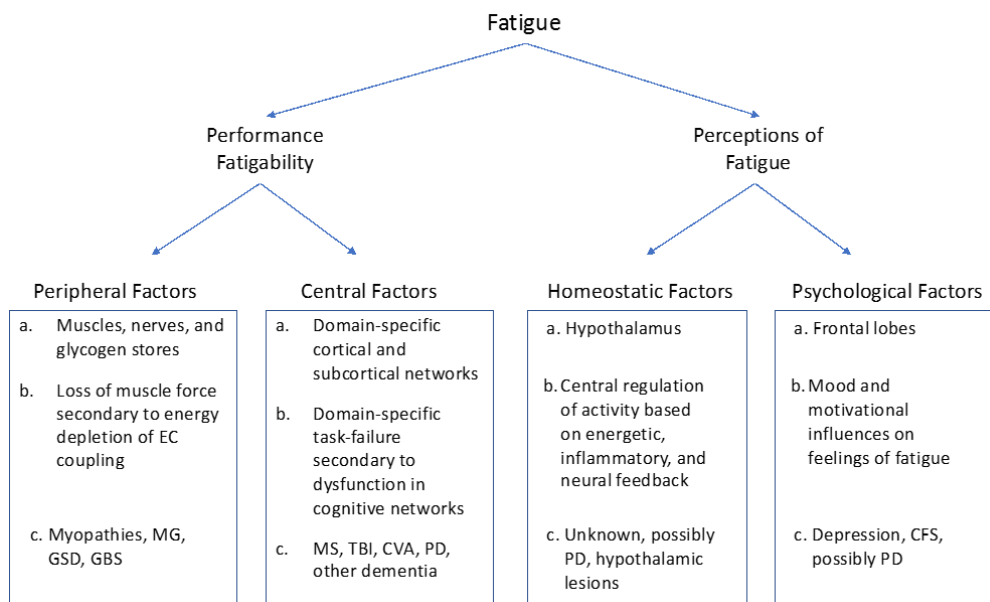
### ***1.3 Swallowing-Related Fatigue: Gaps in Knowledge***

To understand the current state of the field of speech-language pathology regarding clinical perspectives on swallowing-related fatigue, our lab recently conducted a survey of certified SLPs who evaluate and treat adult dysphagia [46]. We found that 86% (n = 311) of SLPs consider fatigue to be an important consideration in dysphagia assessment, and 45% reported explicitly evaluating fatigue during clinical swallowing evaluations. Yet, there was wide variability in how clinicians defined swallowing-related fatigue, indicating disagreement on fatigue definitions and clinical markers. Further, the most common methods for evaluating swallowing-related fatigue were through general, unspecified declines in performance, and via patient report. This lack of specificity and variability in clinical practice reflect a similar lack of standardization for fatigue definitions and measurement methods more broadly across clinical fields [47, 48]. Fatigue is difficult to define and characterize, and its clinical presentations and patient-reported symptoms can vary widely [49].

In treating patients with dysphagia, clinicians may make recommendations such as consuming smaller, more frequent meals to avoid fatigue, and will consider fatigue during dysphagia treatment planning, with such modifications as scheduling sessions at times when patients are less likely to be

tired, and shortening session durations to minimize fatigue effects [50, 51]. In the United States, this practice is supported by the American Speech-Language-Hearing Association (ASHA), which recommends assessing the impact of fatigue on swallowing across different assessment modalities (clinical swallowing evaluations, videofluoroscopic swallow studies (VFSS), and fiberoptic endoscopic evaluation of swallowing (FEES)), but does not specify guidelines or provide resources for how SLPs should do so [52]. Clearly, there is a need to establish a common framework for conceptualizing swallowing-related fatigue to facilitate more accurate identification and measurement of fatigue in the clinical realm, and to guide future research on swallowing-related fatigue and its implications for older and dysphagic individuals.

A framework that may be highly useful for defining and characterizing fatigue in the context of swallowing is that proposed by Kluger, Krupp, and Enoka [53], who outline various factors related and contributing to fatigue (Figure 1). This framework distinguishes between the subjective experience of fatigue, or “perceived fatigue”, and measurable changes in performance, or “performance fatigability” [53]. Factors contributing to perceived fatigue include homeostatic and psychological factors, whereas performance fatigability may have peripheral or central nervous system origins. Though presented as a dichotomy, the framework’s developers note that perceived fatigue and performance fatigability interact with one another (to be discussed in detail later). This framework will serve as a guide through the existing literature on swallowing-related fatigue, and facilitate the identification of gaps in current knowledge.



**Figure 1** Figure adapted from Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. *Neurology*. 2013; 80(4): 409-16, p. 412. Letters in boxes refer to the following: a) known neuroanatomic sites mediating this factor; b) normal function of this factor; c) pathologic states involving this factor. CFS = chronic fatigue syndrome; CVA = cerebrovascular accident; EC = excitation/contraction; GBS = Guillain-Barre Syndrome; GSD = glycogen storage diseases; MG = myasthenia gravis; MS = multiple sclerosis; PD = Parkinson diseases; TBI = traumatic brain injury.

## **1.4 Current Study**

Understanding perceived fatigue and performance fatigability during swallowing will advance clinical management of patients with dysphagia by allowing SLPs to identify and properly manage fatigue-associated risks to swallowing and swallowing-related quality of life. The purpose of this review is to discuss the role of fatigue in swallowing function and eating behavior in the context of aging, propose methods for how fatigue may be measured and managed clinically, and outline implications for future research.

## **2. Performance Fatigability During Swallowing: Quantitative Changes in Performance**

Performance fatigability describes the “magnitude or rate of change in a performance criterion relative to a reference value over a given time of task performance or measure of mechanical output” [53]. Both physical (i.e. motor) and cognitive fatigability can be measured, and both may be relevant to swallowing performance and rehabilitation in elderly adults.

### **2.1 Effects of Motor Fatigability on Swallowing**

Declines in muscle strength with aging have been well established, both in the limbs e.g., [54-56], and in the swallowing musculature e.g., [57, 58]. This may be related to greater age-related atrophy of fast-twitch (type II) fibers compared to slow twitch (type I) fibers in humans [59]. However, less is known about changes in muscle fatigability with aging.

In limb muscle literature, some studies have shown that fatigue resistance is higher in older adults compared to younger adults [60-62], while others demonstrate similar fatigability across ages [63-65], or less resistance to fatigue with aging [66-69]. Conflicting findings may be related to differences in the muscles studied, type of exercise performed (e.g. isometric versus isokinetic), and varied methods of measuring fatigue [70]. Evidence from the limb muscles can be helpful for guiding and informing research on swallowing-related fatigue because limb muscle fatigue has been more heavily studied e.g., [71-73]. However, known differences in muscle composition, morphology, and function limit generalization of these findings to the muscles used during swallowing [31, 74].

Literature on fatigability during swallowing is sparse, and again, the evidence is mixed [75-80]. To date, studies examining swallowing-related fatigability have primarily focused on changes in tongue-to-palate strength and endurance of young and old healthy subjects, although fatigability of suprahyoid musculature involved in upper esophageal sphincter opening has also been studied during the head-lift exercise [81-83]. While this review focuses on swallowing, vocal fatigability is a topic that receives significant attention within the field of speech-language pathology e.g., [84-86] and is mentioned here given the overlapping musculature involved in swallowing and voicing. While an in-depth review of vocal fatigability is beyond the scope of this article, it is interesting to note that similar issues with standardization of definitions, terminology, and clinical identification exist within the field of voice. We direct readers to Welham & Maclagan [87] and Hunter et al. [88] for in depth reviews of vocal fatigue.

For the purposes of this review, we focus the following discussion on studies that have examined lingual fatigability over the course of a meal, followed by studies examining lingual fatigability during intentionally fatiguing exercise tasks.

Given that swallowing is a sub-maximal task, and the orofacial and pharyngeal muscles used during swallowing are predominated by slow-twitch, fatigue-resistant type I fiber types, it is reasonable to expect minimal fatigability of healthy swallowing musculature during a meal. Yet, in older adults, declines in anterior tongue strength over the course of a meal have been reported [76, 89]. Other studies, however, have found no effect of meal consumption on anterior tongue strength in older participants [75], and even increases in tongue strength post-meal [79]. Interestingly, the primary methodological difference between these studies was the type of meal consumed. Both Kays et al. [76] and Brates & Molfenter [89] used a standardized meal consisting of half of a bagel with peanut butter, eight baby carrots, and a thin liquid beverage. The food and liquid textures in this standardized meal are likely more challenging as compared to the meals consumed in studies finding no declines in anterior tongue strength [75, 79], which used meals consistent with participants' normal diets (i.e. less challenging). Across these studies, the only one to find significant declines in posterior tongue strength or endurance after meal consumption was Kays et al. [76]. A conclusion that may be drawn from the available evidence is that elderly, non-dysphagic adults are not at risk for tongue fatigue when eating a meal consistent with their normal diet.

To understand the endurance capacity of the lingual musculature, Solomon et al. [77] had young healthy participants ( $n = 8$ ) perform anterior tongue-to-palate presses until they could no longer sustain 50% of their baseline maximal tongue strength for three consecutive cycles. This fatigue threshold was reached after an average of 31.5 minutes of performing the task. The goal of this study was to explore fatigue-related changes in speech, and thus no swallowing parameters were included as outcome measures. However, the authors found significant differences in perceptual and acoustic speech parameters after the fatigue task.

Vanderwegen and Van Nuffelen [80] used a similar tongue-to-palate lingual fatigue protocol to compare differences in anterior and posterior tongue fatigability in healthy adults across three age groups (20-60 years old,  $n = 20$  and 70+ years old,  $n = 20$ ). In contrast to Solomon et al., no participants ever fell below 50% of their baseline tongue pressures (exercise sessions were aborted after 30 minutes).

In one of the few studies on lingual fatigue in a disordered population, Solomon & Robin [78] compared endurance and perceived effort during tongue-to-palate exercises between people with Parkinson's disease (PD) ( $n = 16$ ) and healthy adults ( $n = 16$ ). Perceived effort was significantly higher in the PD group, and the PD group reached task failure more quickly compared to the healthy group [78]. Taken together, the results of these studies confirm that the tongue is highly resistant to fatigue in healthy, non-dysphagic adults, and possibly less so in dysphagic populations.

Another muscle group that potentially plays a role in swallowing-related fatigue is the postural muscles of the trunk (e.g. external obliques, iliocostalis lumborum pars thoracis, internal oblique, lumbar multifidus, rectus abdominis, and thoracic erector spinae). In our clinician survey [46], some SLP respondents (8%; 8/96) reported postural changes as a clinical indicator of fatigue during swallowing assessments. Postural muscles are activated during upright seated position [90], which is the conventional eating position and is recommended for optimal safety and ease during mealtimes [91]. Fatigue of postural muscles has been demonstrated to negatively affect balance and functional tasks in older people [92]. Yet, the impact of fatigue of postural muscles on swallowing function is currently unknown and warrants further study.

## **2.2 Effects of Cognitive Fatigability on Swallowing**

A discussion about cognitive fatigability and swallowing/mealtime behavior with age is limited to the theoretical and anecdotal realms, given that, to our knowledge, this topic has not been empirically studied. However, the link between cognitive fatigue and swallowing warrants discussion due to the strong theoretical basis for their association.

In addition to requiring muscular endurance, the act of sitting down to independently consume a meal requires a minimum threshold of sustained attention and executive functioning if it is to be performed safely and continuously [93, 94]. Eating a meal is much more than simply chewing and swallowing. It represents an activity of daily living (ADL). ADLs are necessary, everyday behaviors and activities that require adequate executive functioning skills to maintain attention, self-monitoring, self-regulation, and sequencing [95] in relation to homeostatic [96], environmental [97], and psychological factors [98]. Each of these factors represents a possible opportunity for disruption to safe and adequate meal consumption.

The importance of cognitive skills for facilitating safe and efficient swallowing is supported by evidence that dual-task paradigms (i.e. divided attention) can lead to changes in swallowing performance in healthy older individuals [99] and those with Parkinson's Disease [100, 101]. It is also reflected in the common clinical recommendation for patients to avoid distractions (e.g., environmental noise, conversation, interruptions) during mealtimes e.g., [102-104].

Executive control has been shown to decrease with aging, as evidenced by structural and functional neurochemical changes to the frontal lobe [105, 106], with attentional control being an early and highly affected function [107]. Brain regions that are involved in food processing have been found to be strongly modulated by attention focus, including the ventral striatum, premotor cortex, anterior cingulate cortex, insula/frontal operculum, ventrolateral prefrontal cortex and dorsolateral prefrontal cortex [108]. A comparison of swallowing-related brain activity on fMRI between young and old healthy adults has demonstrated increased activity across large regions of the superior and middle frontal lobes in older adults during swallowing, which are cortical areas associated with tasks requiring attention [109].

Cognitive fatigue refers to the effects of prolonged periods of cognitively demanding activity requiring sustained mental effort [110]. Cognitive fatigue can manifest as measurable increases in mental effort, reduced alertness, impaired learning and performance, and stress [111], and also as a lack of motivation and excitement to initiate or sustain task performance [112].

Cognitive fatigability in older adults has been demonstrated after prolonged attention on cognitively taxing tasks [113]. In all humans, cognitive resources are limited and must be allocated effectively and flexibly to adapt to varying cognitive demands. Thus, degraded performance occurs with increasing task demands [114]. While more "automatic" motor tasks such as walking or swallowing are considered to be immune to this type of dual-task deterioration in young and/or healthy individuals [115], increased cognitive demands have been shown to degrade motor performance in older adults [116] and those with neurological impairment/disease [117, 118], due to reduced cognitive resources to begin with, and requirement for more cognitive resources on tasks than would be used by young and/or neurologically healthy individuals. It is possible that the cognitive demands of everyday life may induce fatigue that affects mealtime behavior and/or swallowing performance in older adults and those with neurological disease, including individuals who suffer depression or other psychological disorders [119]. Mental weariness could result in a

lack of motivation to complete a meal and could lead to declines in swallowing performance due to fatigue-induced changes in cognitive functions required for the deglutition process. Risks of cognitive fatigue may be magnified in dysphagic populations who have cognitive impairment (e.g. Alzheimer's Disease, dementia, Parkinson's Disease) and in those who practice recommended feeding strategies and postural maneuvers during meals that may further tax the cognitive system (e.g. performing a chin tuck with every swallow).

The potential relevance of cognitive fatigue further extends to the area of swallowing rehabilitation since therapeutic swallowing exercise programs are often rigorous and require multiple daily sets of varying swallowing exercises. Clinical recommendations often specify that patients should not perform swallowing exercises before meals. In addition to physical fatigue, it is possible that these exercises induce cognitive fatigue that further places patients at risk for impaired swallowing performance. Cognitive fatigue has been demonstrated to degrade neuromuscular performance in older adults [120, 121], therefore effects of cognitive fatigability on motor fatigability of the swallowing mechanism may reduce exercise effectiveness in older patients.

### **3. Perceived Fatigue During Swallowing: Subjective Changes in Performance**

Self-perceived fatigue refers to a person's subjective experience of fatigue, and is best described as a symptom [49, 53]. Fatigue is one of the most common symptoms reported by older adults [47], and self-report is one of the most common methods used by SLPs to identify swallowing-related fatigue, as we have found in a recent clinician survey [46].

There are many available scales and questionnaires that target generalized self-perceived fatigue (e.g. Fatigue Questionnaire [122], Fatigue Severity Scale [123], Multidimensional Assessment of Fatigue Scale [124]), though the operationalization of this symptom varies across scales [125]. Further, clinicians lack standardized methods for defining and identifying self-perceived fatigue [49]. The SWAL-QOL is a validated scale designed to assess dysphagia-related quality-of-life, and includes questions related to fatigue and sleep [126]. However, the creators of this scale note that the fatigue- and sleep-related items are not dysphagia-specific, and are rather designed to capture general quality-of-life factors. Therefore, when patients complain of swallowing-related fatigue, the specific and individualized characteristics of this symptom and how it impacts swallowing and eating experience remains unknown. For example, it is unclear how a sensation of tired masticatory muscles during chewing differentially impacts swallowing and eating compared to feelings of weariness or lack of motivation to eat, and which populations are at heightened risk for each. In order to better understand these factors, swallowing-related fatigue should be investigated with respect to the various dimensions that are traditionally used to characterize clinical symptoms such as pain (e.g. chronology, location, quality, quantity, setting, aggravating or alleviating factors, and associated manifestations) [127].

### **4. Relationship between Performance fatigability and Perceived Fatigue During Swallowing**

Measurable fatigue during performance has not been found to be consistently correlated with the subjective experience of fatigue [128, 129]. In fact, some studies show that young adults, despite having better resistance to fatigability, report higher levels of fatigue than older adults [130, 131]. This may be related to the way individuals self-regulate and control output to stay within a tolerable range of self-perceived fatigue [128]. For example, an individual with a low fatigability threshold



(possibly due to functional impairment) may limit physical output and thus will not reach significant levels of perceived fatigue, whereas an individual with high functional capacity may not restrict physical output and will reach higher levels of perceived fatigue. In the context of swallowing and mealtime behaviors, this may be reflected in food texture and consistency choices, meal preparation time and effort, meal size, and/or meal duration.

A lack of correlation between perceived fatigue and fatigability is also demonstrated in patient populations including stroke [132], myasthenia gravis [133], muscular dystrophies [134], and peripheral neuropathy [134], with patients experiencing fatigue symptoms in the absence of significant measurable fatigue [132-134]. In patient populations, the relationship between these two constructs is complicated by mood and/or psychological conditions related to disease and disability [135], and patients may have difficulty distinguishing between muscle dysfunction due to neurological impairment (e.g. hemiparesis following stroke) versus fatigue symptoms [136]. The lack of correlation between fatigue and fatigability highlights the importance of normalizing measures of self-perceived fatigue to the activity context in which fatigue is experienced and to the specific population of interest.

The exercise physiology literature suggests that measures of self-perceived fatigue, or “sense-of-effort” can be exploited for the purposes of maximizing muscle hypertrophy. Burd et al. [137] compared rates of protein synthesis when healthy subjects performed a leg extension exercise at varying loads (i.e. high load: 90% maximum capacity and low load: 30% maximum capacity) either for a fixed number of repetitions (normalized to load) or until volitional failure (i.e. fatigue threshold). They found that four hours post-exercise, myofibrillar protein synthesis showed a significant and similar response across the two loading conditions when performed to volitional failure, but at 24 hours post-exercise, the protein response was only sustained when the low load (30% of maximum) was performed to volitional failure. A dose-dependent (repetitions x load) effect was seen when repetition rate was fixed. These findings suggest that exercise performed to perceived fatigue is effective for inducing muscle hypertrophy, and lower loads (which can be performed for more repetitions before failure) may be superior to high loads for targeting increased force generation.

The neurophysiological basis for these findings is that, as a muscle fatigues, smaller motor units (innervating Type I slow-twitch, fatigue resistant fibers) cease firing, and larger motor units (innervating Type II fast-twitch, less fatigue-resistant fibers) have to be recruited if the person is to maintain force output [138]. It has been proposed that muscle adaptation is driven by maximum motor unit recruitment and contractile failure [139]. This may be optimally achieved using low-to-moderate loads at high repetitions, to allow time for failure of fatigue-resistant Type I fibers and subsequent recruitment of Type II fibers, which are more responsive to muscle hypertrophy [140].

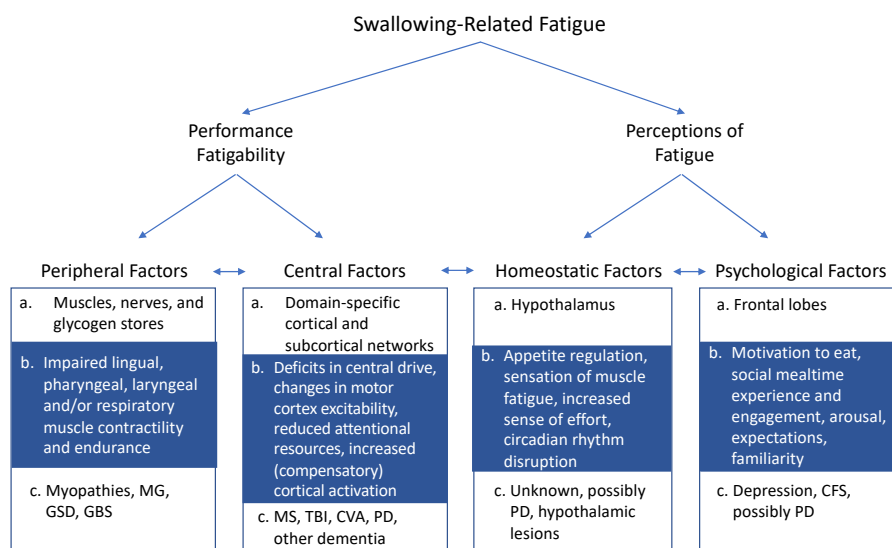
The translation of this evidence to swallowing exercise protocols may be highly useful, given that for many exercises targeting the oropharyngeal musculature, an estimation of load is not practical or feasible in clinical settings, or in prescribed home-based regimens. This problem, and the associated dearth of evidence on optimal dosage for swallowing exercises, likely contributes to the high variability seen in swallowing exercise dosage recommendations [141]. Instead of prescribing a fixed dosage, having patients perform swallowing exercise repetitions until they reach their fatigue threshold (e.g. by using sense-of-effort scales) may improve standardization and tracking of exercise progress, enhance individually-tailored exercise programs, and better facilitate muscle

hypertrophy to improve swallowing outcomes. However, much more evidence is needed to understand the role of self-perceived fatigue thresholds in swallowing rehabilitation and treatment.

### 5. Clinical Implications and Future Directions

Fatigue is a term that is commonly used to describe patient performance and/or subjective experience in the evaluation and management of dysphagia. Given the established association between fatigue and many dysphagia-causing diseases/disorders, SLPs and their professional associations such as ASHA are justifiably aware of and concerned about the potential impact of fatigue on swallowing performance and mealtime behavior. However, there is minimal agreement on and understanding of what constitutes swallowing-related fatigue, how it is identified and measured, who is at risk, and its impact on swallowing function, overall health, and quality of life.

In this review, we have proposed the application of a dichotomous framework [53] for conceptualizing swallowing related fatigue: performance fatigability and self-perceived fatigue symptoms. Given the broad scope of the term “fatigue” and the complexity of what it can describe, we believe that approaching future study and conceptualization of swallowing-related fatigue through this lens is optimal for clearly identifying gaps in current knowledge and designing experimental approaches for resolving them. Figure 2 illustrates a modification of this framework specifically for swallowing-related fatigue, which includes a subset of possible functional changes associated with swallowing-related fatigue that require further study (b). The clinical implications and future directions for each will be discussed in turn, beginning with performance fatigability of the muscles used in swallowing.



**Figure 2** Figure adapted from Kluger BM, Krupp LB, Enoka RM. Fatigue and fatigability in neurologic illnesses: proposal for a unified taxonomy. *Neurology*. 2013; 80(4): 409-16, p. 412. Letters in boxes refer to the following: a) known neuroanatomic sites mediating this factor; b) possible factors associated with swallowing-related fatigue; c) pathologic states involving this factor. CFS = chronic fatigue syndrome; CVA = cerebrovascular accident; EC = excitation/ contraction; GBS = Guillain-Barre Syndrome; GSD = glycogen storage diseases; MG = myasthenia gravis; MS = multiple sclerosis; PD = Parkinson diseases; TBI = traumatic brain injury.

### **5.1 Performance Fatigability: Implications for Swallowing and Future Directions**

Though limited, the current evidence on swallowing muscle fatigability suggests that lingual endurance is very high in non-dysphagic individuals, though the anterior tongue may be more vulnerable to fatigue over the course of a meal in older adults. However, the scope of this conclusion is narrow, and, until further study, its clinical significance is unclear. Some evidence exists to suggest a limited association between anterior tongue strength and functional [142] or physiological swallowing outcomes [143]. Further, it is possible that other muscle groups involved in swallowing (i.e. respiratory, pharyngeal, and/or laryngeal muscles) fatigue before the tongue, resulting in very different consequences to swallowing performance. Imaging studies (e.g. using videofluoroscopy) are needed to investigate whether fatigue-induced changes are manifested as impaired swallowing function (such as aspiration and/or residue) or physiological changes in the pharynx (such as changes in measures of pharyngeal timing and/or extent of structural movement). Research on the effects of respiratory muscle fatigue (i.e. diaphragm, intercostal, and abdominal muscles) on respiratory-swallow patterning is also warranted. Fatigue could potentially disrupt the precise and crucial coordination of swallowing and breathing that is needed for airway protection during swallowing, particularly in populations that demonstrate aberrant respiratory-swallow coordination, such as Parkinson's Disease [144]. Logemann [145] recommended using a "stress test" involving videofluoroscopic observation of pre- and post-meal swallowing performance if fatigue is suspected. This method may be useful for identifying swallowing-related fatigue and its consequences, though there is a need for specification and standardization of criteria for "suspected fatigue", stress test protocols for optimally inducing fatigue, and quantifiable measures for confirming its occurrence.

As illustrated in Figure 2, performance fatigability can be caused by central or peripheral nervous system factors. It is important to distinguish between failures arising centrally versus peripherally as these have different etiologies and implications for rehabilitation. Yet, behavioral tasks such as stress-test protocols or maximal voluntary contractions (MVCs) during tongue-to-palate presses do not allow for distinction between these mechanisms. Solomon [78] has proposed that increased sense-of-effort ratings during tongue presses in adults with Parkinson's Disease may reflect central fatigue processes, given the central pathophysiology of this disease. Etiological information may serve as a helpful starting point for understanding factors involved in swallowing-related muscle fatigue, and muscle groups most at risk for fatigue during swallowing. Looking further, understanding how effects of cognitive fatigability, such as declines in sustained attention, relate to and interact with swallowing performance during a meal, may also help to tease apart central versus peripheral fatigue mechanisms. More research is needed to test these relationships.

The need for quantitative evidence of swallowing-related performance fatigability presents a scientific challenge due to the difficulty of directly measuring fatigue in the pharyngeal, laryngeal, and respiratory musculature. Traditional direct assessment of external skeletal muscle fatigue (e.g. by measuring force output on MVCs or using surface or intramuscular electrodes) is not feasible or ethical for internal application in live human subjects. Use of animal models is a compelling alternative, as is the application of indirect measures of fatigue (e.g. measurement of endurance time or electroencephalogram (EEG) readings). High resolution pharyngeal manometry [146, 147] could also be used to capture changes in pharyngeal pressures as a proxy for fatigue processes. Lastly, quantitative changes in swallowing biomechanics may be compared to measures of self-

perceived fatigue, as has been done previously to understand lingual fatigue in non-dysphagic individuals and those with Parkinson's Disease [78].

Although surface electromyography (sEMG) has previously been used to measure swallowing-related fatigue [75, 81, 83], we caution against this application for two reasons. First, as mentioned, the external placement of sEMG electrodes may not fully capture muscle activity in all the submental musculature used during swallowing (including mylohyoid, geniohyoid, anterior belly of the digastric, and genioglossus), and activation patterns of these submental muscles may vary across individuals [148]. Second, a causal relationship between sEMG output and muscle fatigue is a subject of debate [73]. Studies that pool data across participants have shown that sEMG amplitudes gradually increase across repeated or sustained submaximal contractions [149, 150]. This may be explained by a rise in excitation rates and recruitment of a greater number of muscle fibers to maintain intensity as fatigue occurs [73]. Yet, within-subject data has shown that sEMG amplitudes in limb muscles may rise, fall, or stay the same as a muscle fatigues [151, 152]. This variable sEMG activity has also been observed in head and neck muscles (suprahyoid, infrahyoid, and sternocleidomastoid) during a head-lift exercise [83], with one of five subjects demonstrating large increases in mean frequency rates over the duration of the fatiguing task. This participant was excluded from analyses in this study by White et al. [83] due to these unexpected findings. Because sEMG amplitude represents neural activation (i.e. central fatigue processes), any mechanisms of fatigue occurring within the muscle itself (i.e. peripheral fatigue), which occur *after* the electrical activation that is registered on sEMG, will not be captured. Thus, between-person variability in mechanisms for fatigue, and variable changes in rate of force changes or muscle length during a given exercise task will result in variable fatigue-related sEMG readings. While this may prove useful for understanding central fatigue mechanisms only (and should be explored further), sEMG may not accurately reflect fatigue-induced changes in force output [73].

## **5.2 Perceived Fatigue: Implications for Swallowing and Future Directions**

Our review of perceived fatigue has thus far focused on methods used to capture and assess fatigue symptomology, and its relationship to performance fatigability. In figure 2, we propose possible homeostatic and psychological factors that may contribute to the experience of swallowing and mealtime fatigue that represent areas for future study. The need to understand these factors highlights the complex and multidimensional nature of fatigue, which is represented in Figure 2 with bidirectional arrows between each factor within performance fatigability and perceived fatigue domains. Swallowing-related fatigue must be contextualized within the entire mealtime experience, given the interaction of homeostatic (e.g. hunger) and psychological factors (e.g. mood, motivation) to an experience of fatigue during swallowing. When a patient complains of fatigue during swallowing, there is more to consider than, for example, localized endurance of the lingual musculature. This complexity underscores the relevance of fatigue to the evaluation of dysphagia, which must consider patients holistically, beyond their ability to take a few sips of liquid without aspirating during a brief assessment.

There is a need to establish prevalence and characteristics of perceived swallowing-related fatigue with aging and across different dysphagic populations. Additionally, it is critical to understand the relationship between perceived swallowing-related fatigue and outcomes related to health, nutrition status, frailty status, and quality of life. This information will be useful for the

development of much needed valid, swallowing-specific fatigue scales. Research into perceived fatigue should consider the proposed homeostatic and psychological factors proposed in Figure 2, such as how the mealtime social environment, arousal, mood, and appetite, contribute to feelings of fatigue reported by dysphagic patients. In addition to mealtime adequacy, safety, and health, these are issues that impact quality of life, which is central to the clinical rehabilitation and management of swallowing disorders.

Measures of perceived fatigue (e.g. sense-of-effort scales) should also be used to understand the relationship between perceived swallowing-related fatigue and performance fatigability under imaging, which may help to identify cut-off criteria in sense-of-effort for functional risk. The utility of sense-of-effort scales in swallowing exercise should also be explored to understand whether this can be used to standardize and optimize swallowing rehabilitation protocols.

## **6. Conclusions**

SLPs who evaluate and treat swallowing disorders are trained to consider swallowing performance (i.e. adequate strength, skill, and coordination of the swallowing system to result in safe and efficient bolus passage), within the multidimensional, individualized, and nuanced context in which swallowing occurs. This includes a patient's overall health status and comorbidities, quality of life, personal preferences, cultural norms, and the mealtime context (and associated social context). Fatigue is only one aspect of this complex picture, but may play a role at every level of the swallowing and eating process. As we have discussed in this review, performance fatigability (in both motor and cognitive domains) and perceptions of fatigue are thus relevant to safe, effective, and optimal dysphagia management and rehabilitation, yet need to be further clarified through future study. More immediately and urgently, the establishment of a shared understanding and definition of swallowing-related fatigue, that is recognized and supported by official guidelines, is needed for dysphagia clinical care, both within the field of Speech Language Pathology and across disciplines working with this population. This shared framework will improve awareness and agreement on issues related to fatigue and its role in dysphagia evaluation and management, and will provide a much-needed foundation for future study in this area.

## **Ethics Statement**

No human or animal subjects were involved in this study.

## **Author Contributions**

DB: overall conception, primary role in drafting, and revised manuscript; SM: manuscript conception and revision; MT: manuscript conception and revision.

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The authors have declared that no competing interests exist.

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