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Optimizing Respiratory-Swallowing Coordination in Patients With Oropharyngeal Head and Neck Cancer

Bonnie Martin-Harris,

Roxelyn and Richard Pepper Department of Communication Sciences and Disorders, School of Communication, Northwestern University, Evanston, IL

Kendrea L. (Focht) Garand, and

Department of Speech Pathology and Audiology, College of Allied Health Professions, University of South Alabama, Mobile, AL

David McFarland

School of Speech Therapy and Audiology, Université de Montréal, Montreal, Quebec

Abstract

Swallowing impairment (dysphagia) represents the highest functional morbidity in oropharyngeal (OP) head and neck (HNC) treated either with surgical approaches followed by radiation or with more recent organ preservation protocols, including combined chemotherapy and radiation.

Despite the promising overall increasing survival rates, swallowing impairments remain chronic, are often resistant to traditional swallowing therapy, and have devastating consequences on health and well-being. The respiratory-swallow cross-system approach presented here extends beyond traditional swallowing interventions that commonly targets muscles and structures alone, and is instead, directed toward the re-establishment of optimal respiratory-swallowing coordination.

Results from our work investigating a respiratory-swallow treatment (RST) paradigm is presented, including results from an RST clinical trial in HNC patients, primarily with OP cancers, with chronic and with intractable dysphagia post-cancer and post-traditional swallowing treatment. Future work will investigate the impact of RST on the degree and durability of clinical outcomes, including oral intake and quality of life, while also examining the potential added benefits of a home practice program that uses a commercially available and easy to use recording and analysis hardware and software.

An estimated 350,000–400,000 people are diagnosed worldwide with oropharyngeal (OP) head and neck cancer (HNC) each year—nearly 10% of these in the United States alone (Altekruse, et al., 2010). Unlike many other cancers, the incidence of OP HNC is moving in the wrong direction—an increase of 1.3% from 2007 to 2011 likely related to tumors incited by the human papilloma virus (HPV-positive; American Cancer Society, 2015; Gillison, Chaturvedi, Anderson, & Fakhry, 2015). Swallowing impairment (dysphagia) represents the highest functional morbidity in OP HNC treated either with surgical

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approaches followed by radiation or with more recent organ-preservation protocols, including combined chemotherapy and radiation (Gillespie, Brodsky, Day, & Martin-Harris, 2004; Gillespie et al., 2005; Hutcheson, Yuk, Holsinger, Gunn, & Lewin, 2015; Lazarus et al., 2000). Swallowing impairments remain chronic, are often resistant to traditional swallowing therapy, and have devastating consequences on health and well-being.

Refinement and modification of traditional therapy paradigms to treat swallowing impairments associated with OP HNC are slowly emerging and show potential toward reversing some of the devastating effects associated with radiation and chemotherapy (Carnaby-Mann & Crary, 2010; Carnaby-Mann, Crary, Schmalfuss, & Amdur, 2011; Crary, Carnaby, LaGorio, & Carvajal, 2012; Govender, Smith, Taylor, Barratt, & Gardner, 2017; Lan et al., 2012; Lazarus, 2006; Lazarus et al., 2007; Virani, Kunduck, Fink, & McWhorter, 2015; van der Molen, van Rossum, Smeele, & Hilgers, 2014). The respiratory-swallow cross-system approach presented here extends beyond traditional swallowing interventions that commonly target muscles and structures alone, and is instead, directed toward recalibration of respiratory-swallow phase patterning. Our clinical trial work has demonstrated improvements in respiratory-swallowing coordination may improve many physiologic mechanisms that are fundamental for safe and efficient swallowing (Martin-Harris et al., 2015). With previous and ongoing work, we propose that persistent swallowing impairment may be due not only to disordered physiological processes within the oral and pharyngeal domains, but also may be negatively impacted by disrupted cross-system coordination with breathing. The underlying nature of the dysphagia may predispose certain patients to disruptions in the otherwise highly stable respiratory-swallow coupling observed in typical, nondysphagic persons (Brodsky, et al., 2010; Martin-Harris et al., 2015; Martin-Harris et al., 2005).

A substantial body of literature, including our own work, using a variety of measurement techniques, including respiratory airflow, rib cage and abdominal movements, and motion imaging of the upper aerodigestive tract has established this highly stable respiratory-swallowing coordinative relationship in normal individuals (Hiss, Treole, & Stuart, 2001; Martin-Harris et al., 2005; Preiksaitis, Mayrand, Robins, & Diamant, 1992; Nishino, Yonezawa, & Honda, 1985; Selley, Flack, Ellis, & Brooks, 1989). Precise respiratory-swallow coordination is vital for airway protection since respiration is inhibited before and during pharyngeal swallowing in all species, including infant and adult humans (McFarland & Lund, 1993; McFarland & Lund, 1995; Martin, Logemann, Shaker, & Dodds, 1994; Nixon, Charbonneau, Kermack, Brouillette, & McFarland, 2008; Palmer & Hiimae, 2003; Paydayfar, Gilbert, Poppel, & Nassab, 1995; Smith, Wolkove, Colacone, & Kreisman, 1989). In a recent large-scale study of healthy, nondysphagic individuals swallowing upright consuming a variety of different bolus characteristics and methods of delivery, we have shown that swallowing consistently occurs during mid-to-low quiet breathing expiratory lung volumes. We have argued that this optimal respiratory-swallowing coordination imparts important airway and mechanical advantages for swallowing (Charbonneau, Lund, & McFarland, 2005; Martin-Harris et al., 2015; McFarland, Lund, & Gagner, 1994). This partly revolves around the activity of the diaphragm, and the traction it puts on upper airway structures during breathing. The diaphragm, which descends to contraction to increase the superior inferior and lateral anterior dimensions of the lungs/thorax, continues to be active

during the early expiratory phase of the breathing cycle to slow the return of the lungs thorax unit to its rest position at end expiratory lung volumes (Agostoni & Mead, 1964). The diaphragm is at its most superior, relaxed position at end expiratory lung volumes, which may facilitate pharyngeal shortening, laryngeal elevation, pharyngoesophageal segment opening, and distal esophageal bolus clearance into the stomach (Agostoni & Mead, 1964; Trop, Baert, & Van de Woestijne, 1967). Similarly, swallowing at mid-to-low quiet breathing expiratory lung volumes assures that the traction placed on the larynx is minimal, and this may assist in the crucial airway protection functions of laryngeal elevation and also contributes to pharyngoesophageal sphincter opening. Further, mid-to-low expiratory phase of the quiet breathing is associated with medialization (paramedian position) of the vocal folds (Martin et al., 1994). This laryngeal posture during expiration provides an advantageous set point for further glottal closure required to protect the airway during swallowing. Our work and others have suggested the positive pressure associated with the brief post-swallow expiration may facilitate sensation of residue in and around the laryngeal inlet and therefore, trigger protective expectoratory maneuvers (e.g., throat clear/cough) after the swallow (Martin et al., 1994; Nishino et al., 1985; Paydarfar et al., 1995).

Nonoptimal respiratory-swallow phase patterning (e.g., swallowing at a high lung volume during inspiratory phase) has been observed in patients with OP HNC and dysphagia (Brodsky et al., 2010). We have hypothesized that this may be due to: (a) impairments within the oropharyngeal swallowing system, such as delayed initiation of the pharyngeal swallow, reduced tongue base retraction, and impaired pharyngeal shortening and laryngeal elevation; (b) within the respiratory system that impact coordination with swallowing; and/or (c) within neural control resulting in disruption of respiratory-swallow phase stability. This led to the development of the theoretical context for examining both “within” (swallowing impairment) and “across” (respiratory-swallow patterning) systems.

RST in HNC

We then developed a visually-directed biofeedback training regimen in patients who demonstrated suboptimal patterns and longstanding dysphagia (Martin-Harris et al., 2015) (Figure 1). The RST program was developed using a hierarchical training supported by principles of motor learning and neural plasticity (Bloom, 1956; Bloom, 1968; Krathwohl, Bloom, & Masia, 1956). The RST protocol was divided into 21 goals distributed among three learning modules: Identification, Acquisition, and Mastery. For each goal within the Identification and Acquisition module, 80% accuracy in trials was required for the goal to be met (Figure 1). A 90% accuracy was required during the mastery module. Liquid boluses provided during RST were only given for liquid consistencies with Penetration/Aspiration Scale (PAS) scores ≤ 6 identified on the pre-RST videofluoroscopic imaging (modified barium swallow study [MBSS]).

During the Identification module, quiet breathing respiratory signals were presented on laminated cards by the training speech-language pathologist and patients were trained to accurately identify respiratory phases on command (inspiratory and expiratory). The patient was then instructed to identify the mid-to-low lung volume range of the expiratory phases of the respiratory cycle depicted on the respiratory signal examples. Next, the patient learned to

identify these targets of the respiratory signal on a computer monitor that they watched during their actual breathing recorded and calibrated using respiratory inductance plethysmography. Patients then progressed to implementing the optimal respiratory-swallow phase pattern (swallows initiated in the expiratory phase of respiration in the mid-to-low lung volume range followed by expiration) during natural cup drinking of graduated volumes and consistencies of liquid. Only liquid consistencies that received a score of 6 on the Penetration-Aspiration Scale (i.e., if aspirated were expectorated; Rosenbek, Robbins, Roecker, Coyle, & Woods, 1996) observed on the baseline videofluoroscopic studies were used during the respiratory-swallow training. Each RST session lasted approximately one hour, with two sessions scheduled each week. Patients were purposely not instructed to practice at home in this preliminary trial because there was not a reasonable method to ensure compliance. Our planned trial, however, is specifically designed to examine the potential augmentative treatment effect of home training.

We tested this innovative treatment procedure in 30 patients who were at least six months posttreatment (medical/surgical/swallowing) for HNC, primarily OP, and presented with ongoing dysphagia. Patients were included if they demonstrated both swallowing impairment refractory to prior swallowing treatment and nonoptimal respiratory-swallow phase patterning as observed on a baseline assessment using simultaneous videofluoroscopy and calibrated respiratory recordings during a modified barium swallowing study that included graduated volumes and consistencies of standardized liquid barium (i.e., thin, nectar-thickened, and honey-thickened; Martin-Harris et al., 2015; Bracco Diagnostics, Inc.; VARIBAR®). Solids were not given because of the airway protection concerns in these patients, some of whom presented with marked pharyngeal clearance deficits. In this baseline study, patients were not instructed to swallow in any particular way or in any particular respiratory phase, but rather to take the liquids and swallow them in their usual manner.

The goal of the study was to (a) determine if the optimal respiratory-swallow pattern could be trained; and if acquired, to (b) determine if the optimal pattern had a positive outcome on physiologic swallowing components, airway protection and swallowing specific quality of life. As such, the primary study outcomes were: (a) respiratory-swallow phase patterning, (b) Modified Barium Swallowing Impairment Profile (MBSImP) scores (Martin-Harris et al., 2008), (c) PAS scores (Rosenbek et al., 1996), and (d) M. D. Anderson Dysphagia Inventory (MDADI) scores (Chen et al., 2001).

Results revealed that it took an average of six RST sessions to reach mastery (Martin-Harris et al., 2015). All 30 patients underwent a post-RST MBSS in a median of 4.5 days of the final RST session, and 15 of the 30 patients also participated in another MBS at one month post-RST to explore any detraining effects. Patients were not coached during the MBS and followed the same liquid swallowing protocol used in their baseline assessment. Results showed that optimal phase patterning increased significantly after the RST intervention ($p < 0.0001$; Table 1). That is, all patients learned to recalibrate their respiratory-swallow phase patterning to produce the optimal pattern of initiating the swallow during mid-to-low lung volume of the expiratory phase followed after the swallow by expiration. Furthermore, there were improvements in three of the MBSImP component scores compared with pre-RST

scores: laryngeal vestibular closure ($p = 0.0004$), tongue base retraction ($p < 0.0001$), and pharyngeal residue ($p = 0.01$). Significant improvements were also seen in PAS scores following RST ($p < 0.0001$). Relative to pre-RST values, patients participating in one month follow-up ($n = 15$) demonstrated stability in the learned optimal RST phase pattern, PAS scores, and MBSImP scores observed during post-RST MBSS. Further, MDADI scores also significantly increased after RST, although this did not reach the clinical relevant difference of a 10-point change (Hutcheson et al., 2015; Table 1). These findings suggest that patients with OP HNC and refractory dysphagia could be trained successfully to produce an optimal respiratory-swallow phase pattern after completion of a structured training protocol (RST) and that there were positive effects on mechanisms of bolus clearance and airway protection during liquid swallowing.

Toward further validation of our treatment effect, Pearson and colleagues (2016) examined 192 pre- and post-RST swallows from nine of the patients in the RST intervention trial that demonstrated improvement in laryngeal vestibular closure using computation analysis of swallowing mechanics (CASM)—multivariate morphometric analysis of coordinates mapping the functional anatomy related to swallowing observed on videofluoroscopic imaging. CASM revealed statistically significant differences in pharyngeal swallowing mechanics between pre- and post-RST groups (mean patient-specific analysis, $D = 3.33 \pm 0.90$, $p < 0.0001$; aggregate data analysis, $D = 0.80$, $p < 0.0001$). Additionally, regression analysis indicated that pharyngeal swallowing mechanics associated with RST was predictive of mechanics associated with laryngeal vestibular closure in the aggregate ($R^2 = 0.25$, $p < 0.000$).

We proposed the swallowing at mid-to-low lung volume in the expiratory phase of the respiratory cycle imposes significant physiologic advantages for airway protection and swallowing efficiency. Our findings that showed improvements in laryngeal vestibular closure and pharyngeal clearance support this hypothesis. Future studies employing a randomized trial design and a control group will further inform investigators and clinicians of the targeted effects of RST on these and other components of the swallowing mechanism.

Conclusions

Despite important advancements in medical and surgical treatments that prolong survival, individuals with OP HNC are faced with chronic dysphagia resulting in drastic alterations in diet, the need for feeding tubes, and increased risk for aspiration pneumonia and associated life-threatening complications. The results from our preliminary study using a novel and theoretically-driven approach, RST show potential for high impact when recalibration of respiratory-swallowing coordination can be learned by patients with OP HNC.

Our next clinical efficacy RST trial is designed to further investigate the impact of RST on the degree and durability of not only physiologic swallowing outcomes, but also clinical outcomes including oral intake and quality-of-life. Further, we will also examine the potential added benefits of a RST home practice program that uses a commercially available recording and analysis hardware and software. Consistent with our clinical research track records, our goal is to clinically translate our experimental findings into turn-key,

standardized, and reproducible treatment programs to improve the quality of life of our patients with HNC and other dysphagia patient groups shown to present with suboptimal respiratory-swallow patterns.

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Figure 1.
Depiction of Goals for Each Training Module and Intervention Timeline.

Table 1

Pre- and Post-RST Rates for the Following Outcome Measures: Respiratory-Swallow Phase Pattern, Impaired PAS Scores, Impaired MBSImP Scores, and Average MDADI Scores.

Outcome Measure	Pre-RST	Post-RST	<i>p</i> -value
Optimal respiratory-swallow phase	43.0	86.0	<0.0001
Impaired PAS scores (3)	78.0	38.3	<0.0001
Impaired MBSImP Component Scores *			
Lip closure (2)	5.7	9.3	0.17
Tongue control during bolus hold	58.7	53.8	0.14
Bolus transport/lingual motion	37.3	50.2	0.07
Oral residue (2)	77.3	76.4	0.80
Initiation of pharyngeal swallow	90.4	90.8	0.87
Soft palate elevation	19.8	31.0	0.03
Laryngeal elevation	76.6	70.8	0.43
Anterior hyoid excursion	94.7	90.5	0.10
Epiglottic movement	71.9	68.3	0.31
Laryngeal vestibular closure	78.2	55.5	0.0004
Pharyngeal stripping wave	59.3	67.6	0.27
Pharyngoesophageal segment opening	80.6	80.5	0.99
Tongue base retraction 2	96.0	88.6	<0.0001
Pharyngeal residue 2	96.1	88.4	0.01
MDADI (mean ± SD)	60.4 ± 14.8	65.3 ± 16.7	0.003

Note.

* Unless otherwise stated, MBSImP scores of 1 were considered impaired.