Clinical Implications of Cross-System Interactions

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ABSTRACT

In this review, we briefly highlight potential cross-system interactions between swallowing and speech production, using data from recent neuroimaging studies, common clinical impairments, cross-system treatment effects, and developmental considerations as supporting evidence. Our overall hypothesis is that speech and swallowing (and other motor behaviors) are regulated through a shared network of brain regions and other neural processes that are modulated on the basis of specific task demands. We emphasize the clinical utility of viewing speech and swallowing as being closely linked from both a diagnostic and treatment perspective. We stress the importance of continuing research to explore the common and perhaps distinct neural circuitry underlying speech and swallowing and the clinical intervention strategies that attempt to capitalize on potential cross-system therapeutic benefits.

KEYWORDS: Cross-system interactions, speech, swallowing

Learning Outcomes: As a result of this activity, the reader will be able to (1) describe the complexity of the swallowing control processes, the relationship to speech production, and the common neural control mechanisms underlying both behaviors; and (2) explain the potential clinical importance of viewing swallowing and speech (and other motor behaviors) as closely linked from a diagnostic and treatment perspective.

Swallowing is an extremely complex sensorimotor behavior involving coordinated activity in a vast array of muscles distributed across several physiological systems including the respiratory, laryngeal (phonatory), and masticatory (oral-articulatory) systems. Multiple neural control elements regulate this complex dynamic including central pattern generating circuitry, sensory feedback, and other subcortical and cortical control processes. Masticatory,

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New Frontiers in Dysphagia Rehabilitation; Guest Editor, JoAnne Robbins, Ph.D., CCC-SLP, BRS-S.

Semin Speech Lang 2006;27:300–310.

DOI 10.1055/s-2006-955119. ISSN 0734-0478.

respiratory, and laryngeal systems also participate in speech production, and speech and swallowing share some if not much of their neural control elements. It is not surprising, therefore, that disease and damage may simultaneously affect speech and swallowing and that important diagnostic information may be gained by looking at common impairments.

Neuroscientists and others have questioned the rather long-standing belief that control properties underlying motor behaviors, particularly those from apparently divergent motor systems, are distinctly represented in the nervous system.[1–3] Instead, although some unique control elements may exist for specific behaviors, our emerging understanding of motor function is of mutual interactions and common control elements.[1,4] There is converging clinical and research evidence that speech and swallowing may share these types of common interactions, and consequently, attempts to separate them from either a diagnostic or treatment perspective may be neither valid nor clinically useful. Although it is beyond the scope of the present review, the consideration of cross-system effects has extended beyond motor systems to include perception–action coupling[5] and interactions between cognitive linguistic elements and motor function underlying the production and development of normal and disordered speech production.[6,7]

In this review, we provide a brief introduction to the cross-system association of swallowing and speech (and other motor behaviors), highlighting shared control elements and clinical consequences. Our goal is to explain the utility of viewing speech and swallowing as being closely linked from both diagnostic and treatment perspectives.[8] This approach is critical as our population ages and as the effects of age-related disabilities in speech and swallowing[9,10] place additional burdens on health care delivery.[11]

SWALLOWING AND ITS NEURAL CONTROL

Brainstem Pattern Generation

Swallowing has the double function of transporting food and saliva and providing airway protection during both wakefulness and sleep. This highly complex coordinated process involves multiple levels of nervous system function including central pattern generating circuitry interacting with sensory feedback and cortical control elements.[12–16] Much research attention has been given to identifying and characterizing the brain stem pattern-generating circuitry responsible for the basic swallowing pattern.[13,17] Like breathing, chewing, and walking, interneurons have been identified in the brain stem that are capable of generating a basic swallowing pattern in the absence of ascending (sensory) or descending (e.g., cortical) inputs. These neural networks are referred to as central pattern generators. The swallowing central pattern generator is sometimes erroneously interpreted as containing all of the neural circuitry to generate the swallowing "reflex" (i.e., the pharyngeal phase of swallowing). Classically, central pattern generators have been thought of as anatomically distinct interneurons generating rhythmic or repetitive motor outputs.[18,19] More recently, they are being conceptualized as flexibly organized neural networks with multifunctional neurons that are biased to produce task-specific motor behaviors.[13,20–26] This flexible organization underlies not only the coordinated activity within the swallowing system but also the tight neural cross-system coordination with respiratory and laryngeal systems.[13,27–29] Normal swallowing occurs at precisely timed moments in both the respiratory and masticatory movements.[30–32] Respiration is inhibited, and swallowing occurs consistently at the end expiratory phase of the breathing cycle in adult humans swallowing solid food boluses.[29,30,33–35] The tight temporal relationship between breathing and swallowing remains despite major modifications to upper airway structure and function, indicating tight neural coupling between respiratory and swallowing neural processes.[21]

Vocal fold closure, laryngeal elevation, and velopharyngeal closure combine with respiratory inhibition to protect the airway during swallowing.[36–38] End expiratory timing of swallowing facilitates laryngeal elevation for airway protection and cricopharyngeal sphincter opening for bolus transport.[21,31] Swallowing occurs within a pause in the masticatory sequence with the jaws slightly open, providing an appropriate biomechanical platform for bolus movement to the pharynx.[17,32] As a consequence, respiratory, laryngeal, and masticatory (oral-articulatory) processes must be precisely coordinated for appropriate swallowing function. This emphasizes not only the complexity of the normal swallowing process but also the clinical necessity of taking into account cross-system coordination in both the diagnosis and treatment of swallowing disorders.[39]

Sensory Feedback and Cortical Control Processes

As in other centrally patterned movements, sensory feedback is crucial for the modification of the basic swallowing pattern for changing internal and external conditions. It is well known that sensory receptors located in the oral-pharyngeal cavity are responsible for the initiation of the pharyngeal phase of swallowing. Less well known is the important contribution of sensory control processes in regulating and adapting swallowing function for changing environmental constraints. For example, increases in bolus volume and consistency changes the timing and pattern of all phases of swallowing, including the pharyngeal and esophageal components that are often thought to be independent of feedback and reflexive in nature.[40–46] Feedback from respiratory volume and phase sensors also feed to swallowing control processes, indicating an even broader effect of sensory feedback on control processes.[31,47] Cortical control processes are crucially important in the interpretation of these sensory regulating signals and in the modification of basic pattern generation in response to changing physiological and mechanical constraints. Cortical lesions, as a consequence, negatively affect all aspects of the swallowing synchrony including pharyngeal and esophageal control processes.[15] Swallowing, therefore, is not a reflex but instead a complex coordinated process produced by multiple levels of neural control distributed across several key physiological systems. Understanding the underlying pathophysiology and neural control parameters is crucial if we are to be able to properly diagnosis and treat swallowing disorders.[39,48,49]

SPEECH AND SWALLOWING

The same systems involved in swallowing also participate in the production of speech[1] (for a review, see McFarland and Lund[17]). The respiratory system provides the driving force for sound production, the laryngeal system provides the voice source through vocal fold vibration, and the oral-articulatory system shapes the sound generated by the vibrating folds to produce specific speech sounds.

Clearly, like swallowing, the neural control processes involved in speech production are diverse and include higher-level motor control as well as brainstem and cerebellar systems and feedback from a variety of sensory afferents.[50] Sensory inputs including audition are crucially important for speech development,[51–53] and for the modification of speech movements in response to structural or functional perturbations to control processes, such as those related to changes in oral form and function.[54]

The fact that common systems/muscles are used for speech production and feeding/swallowing indicates a high degree of at least peripheral motor control overlap. This cross-system interaction, however, extends to much higher levels of motor control and coordination. Here we suggest that the oral-facial-laryngeal system is organized in a manner that is largely task independent (or integrative), through a shared network of brain regions that is modulated by task demands.[55] The alternative hypothesis is that task-specific speech or swallowing movements of the oral-articulatory, laryngeal, and respiratory structures are controlled through distinct and largely nonoverlapping neural networks.[56] Recent imaging studies, however, have revealed that swallowing is controlled through a network of cortical areas that is far more distributed than traditionally assumed[57–62] and that this network appears to be common to other movements including speech production. For example, using functional magnetic resonance imaging techniques, Martin and colleagues[60] compared brain activation associated with swallowing, tongue movements, and thumb-to-finger contact. Subjects were instructed to swallow accumulated saliva (during a 2-minute trial period), raise the tongue to the palate and maintain this position for 2 seconds, and alternately oppose the finger to the thumb at a rate of two times per second. Results showed large regions of brain activation common to swallowing and tongue movement (over 1200 mm^3) and, to a lesser extent, between swallowing and oppositional finger movements (69 mm^3). There were also regions of overlap between tongue and finger movements (267 mm^3). Activity in the supplementary motor area and in the anterior cingulate area (Brodmann areas [BA] 32/24) was found for all motor tasks. Additional regions common to swallowing and tongue movements included the postcentral gyrus (BA 3 and 4), the cuneus and precuneus, and the supramarginal gyrus. A subsequent functional magnetic resonance imaging study conducted by the same group[62] further demonstrated that swallowing accumulated saliva is associated with activity in the primary motor and primary sensory areas, in the insula, and in the anterior cingulate. These results are largely consistent with results of other studies of voluntary swallowing conducted in different laboratories.[57–59,63]

Other studies have looked at the potential overlap in the cortical representation of speech and other orofacial movements.[64–66] For example, Saarinen et al[66] used magnetoencephalography to study activity in the primary motor area for speech (phoneme and word production), as contrasted to a series of matched orofacial movements involving the lips, the tongue, or the mandible. Results showed that the time-course and amplitude of the rhythmic activity in the β band in the face representation of the primary motor area was nearly identical for all the tasks.

Taken together, the results of these and other imaging studies indicate a complex system of neural control elements that is common to speech, swallowing, and other orofacial movements. This includes the primary motor and the primary somatosensory areas, as well as other regions such as the supplementary motor area, the anterior cingulate area, the insula, and the cerebellum.[58,60,61,64,67,68]

Most if not all of these brain regions (with the possible exception of the insula) also contribute to the production of other complex movement sequences in addition to swallowing and speech production, such as finger and reaching movements.[69–71] For example, although Broca's area has traditionally been thought of as being exclusive to speech production, recent imaging and lesion studies have revealed this area to be importantly involved in a wide range of tasks including object manipulation,[72] finger movement execution and imagination,[73] action imitation,[74,75] observation of object-related mouth movements (biting an apple and chewing), and object-related hand/arm movements (reaching and grasping a ball or a little cup with the hand).[76] Potentially shared neural elements lead to the prediction that there might be mutual interactions between apparently divergent motor behaviors, such as speech and other whole-body movements. To investigate these potential interactions, Gentilucci et al[1] had subjects produce several tasks involving reaching at and grasping an object of different sizes while simultaneously opening the mouth or pronouncing a syllable. Reaching and grasping the larger object resulted in increased lip opening and vocal loudness when contrasted with the smaller-object manipulation, suggesting cross-system interactions in amplitude scaling across these seemingly different motor behaviors.

Developmental Interactions

Additional motivation for considering potential cross-system interactions between speech and swallowing/feeding comes from a developmental perspective. Swallowing is observable in the developing fetus by the twelfth week. In fact, swallowing is crucial for the regulation of amniotic fluid in the developing infant.[77,78] At birth, the infant must make the transition between swallowing in a liquid environment to integrating swallowing with airway-protective mechanisms. Swallowing and its coordination with breathing (and sucking) are unstable at birth and develop postnatally. Sensory feedback, experience, and neural maturation combine to encourage the maturation of feeding and swallowing. Experience is crucial, and there are critical and sensitive periods of swallowing development during which experience-related feedback is necessary for normal development.

For example, newborns that are tube fed for prolonged periods have difficulty in the normal development of liquid and bolus swallowing.[79] It is well known that there are similar critical or sensitive periods in speech/language development.[80] Extending the concept of sensitive or critical periods, much experimental and clinical attention has been given to the potential interdependence of communicative development on appropriate feeding and swallowing progression in infants and children. That is, normal feeding and swallowing development may be important precursors for appropriate speech language development. In fact, feeding and swallowing difficulties together with other neurodevelopmental factors may provide important early-detection indicators for later speech and language difficulties in developing infants.[81] This places additional importance on the mutual consideration of speech and swallowing impairments.

At the other end of the spectrum, there are a variety of changes in swallowing control and function related to normal aging that must be taken into account when considering disordered function consequent to disease and stroke.[39,44,82] These include changes in muscle function and coordinative timing among swallowing events (including the coordination with respiratory processes). Further, response to behavioral intervention based on the neural plasticity of affected neural structure and function (the basis of all neurorehabilitation) has been shown to be age dependent, decreasing with advancing age.[83,84]

Clinical Evidence of Cross-System Interactions

We now turn our attention to additional considerations of potential cross-system interactions between speech and swallowing as revealed by the co-occurrence of speech and swallowing impairments.

There is a great deal of evidence of the co-occurrence of voice/speech and swallowing impairments.[85–90] Martin and Corlew[91] studied the co-occurrence of swallowing disorders and speech/language impairments in 115 patients in Veteran's Administration Medical Center (a long-term care facility) with radiographically confirmed swallowing impairments. Of all patients, 93% of those presenting swallowing impairments also had co-occurring speech disorders. A retrospective follow-up study of 91 patients in an acute care setting by Lapointe and McFarland[8] revealed that 79% of all patients judged to have swallowing impairments also presented communication disorders.

The relationship between speech disorders and swallowing impairments is not a simple one and requires a detailed understanding of the nature of the neurological impairment as well as of the specific speech impairment. For example, Nishio and Niimi[89] assessed the correlation between measures of speech intelligibility and swallowing disorders in 113 dysarthric speakers. A very high correlation was found between decreased speech intelligibility and the presence of swallowing impairments. However, the prevalence and level of severity of swallowing disorders differed between dysarthria types, arguing for a thorough understanding of underlying speech motor disorders as potential correlates of swallowing disorders.

The co-occurrence of swallowing and speech impairments indicates common or at least overlapping pathology. Therefore, it seems reasonable to assume that therapeutic intervention targeting one or both of the systems may have cross-system or perhaps complementary effects.[92] In a recent preliminary treatment study, El-Sharkawi et al[93] applied well-established speech/voice treatment to patients with swallowing disorders. This treatment, the Lee Silverman Voice Treatment, involves the recalibration of a patient's sensorimotor system with intensive vocal exercises focusing on increased loudness. Such treatments were designed for and typically applied to patients with Parkinson's disease to improve their loudness and communicative effectiveness. Videofluoroscopic results revealed more efficient swallowing in the swallowing-disordered patients subsequent to this speech treatment.

These and other treatment data from divergent motor systems indicate the potential utility of cross-system treatment effects, and they reinforce the clinical importance of viewing speech and swallowing impairments within a global motor control context. The clinical implications are evident. The tight correlation between speech and swallowing impairments has important diagnostic significance. The presence of one of these disorders may signal the presence of another. In fact, anecdotal clinical evidence indicates that specific voice disorders are so highly correlated with swallowing impairment that speech-language pathologists immediately refer susceptible patients for more detailed swallowing exams when their disorders are detected by careful speech-language examination. However, the inverse is less commonly appropriate; that is, the presence of a swallowing problem does not as frequently trigger a consult for voice evaluation. Nonetheless, the complex nature of swallowing impairments and their potential relationship to speech production, including developmental factors, argues for a thorough understanding of the anatomy, physiology, and neural control processes underlying both of these motor behaviors. Understanding the underlying pathology may provide important treatment directions and increase treatment efficacy. Given the fact that there are multiple points of potential cross-system interaction, treatments targeting one system, such as speech, may have important distributed effects and improve swallowing function. That is, treatments may have a more "global" effect that traverses the specific targeted function.

One obvious extension of the potential transference of treatment effects from one motor behavior to another (such as speech to swallowing) is to target each impaired function simultaneously in the same clinical session. That is, to provide highly specific and functionally relevant treatment tasks directed at each "system" but with a common treatment goal. Such complimentary treatment regimes have recently been developed based on the Lee Silverman Voice Treatment for Parkinson's disease, in which speech and whole-body movements (such as reaching) are trained simultaneously and with the overall treatment goal of increasing movement amplitude across these apparently divergent motor systems.[94–96] Clearly, the potential clinical benefit of cross-system interactions, or complimentary effects of common treatment protocols, will depend in as-yet-unknown ways on a variety of disease parameters including type, severity, time post-onset, patient age, and other concurrent impairments. As highlighted in this brief review, the numerous points of interaction within the nervous system underlying presumably diverse motor behaviors such as speech and swallowing argues for continued investigation of the clinical utility of cross-system treatment interactions.

SUMMARY

We have briefly reviewed the complex neurological mechanisms involved in the control and coordination of swallowing. We have discussed that normal function involves several levels of nervous system activity including pattern-generating circuitry, cortical mechanisms, and sensory feedback. We provided a brief review of common underlying control processes involved in both speech and swallowing, the co-occurrence of swallowing and speech/language impairments related to disease and damage, and the potential clinical benefit of treating swallowing and speech/language disorders within a global motor control construct.

ACKNOWLEDGMENTS

This work was supported in part from grants from the National Science and Engineering Council of Canada. We thank numerous colleagues for their thoughtful discussions of the current and related topics.

REFERENCES

1. Gentilucci M, Benuzzi F, Gangitano M, Grimaldi S. Grasp with hand and mouth: a kinematic study on healthy subjects. J Neurophysiol 2001;86(4): 1685–1699
2. Smith A, McFarland DH, Weber CM. Interactions between speech and finger movements: an exploration on the dynamic pattern perspective. J Speech Hear Res 1986;29(4):471–480
3. Kelso JA, Holt KG, Rubin P, Kugler PN. Patterns of human interlimb coordination emerge from the properties of non-linear, limit cycle oscillatory processes: theory and data. J Mot Behav 1981;13: 226–261
4. Gentilucci M. Grasp observation influences speech production. Eur J Neurosci 2003;17(1):179–184

5. Rizzolatti G. The mirror neuron system and its function in humans. Anat Embryol (Berl) 2005; 210(5–6):419–421
6. Goffman L. Kinematic differentiation of prosodic categories in normal and disordered language development. J Speech Lang Hear Res 2004; 47(5):1088–1102
7. Weber-Fox C, Spencer RM, Spruill JE III, Smith A. Phonologic processing in adults who stutter: electrophysiological and behavioral evidence. J Speech Lang Hear Res 2004;47(6):1244–1258
8. Lapointe J, McFarland DH. Pourquoi les orthophonistes devraient-ils s'intéresser à la dysphagie? Frequence 2004;16:22–25
9. Ruber RJ. Redefining the survival of the fittest: communication disorders in the 21st century. Laryngoscope 2000;110:241–245
10. Schindler JS, Kelly JH. Swallowing disorders in the elderly. Laryngoscope 2002;112:589–602
11. Byles J. The epidemiology of communication and swallowing disorders. Adv Speech Lang Pathol 2005;7:1–7
12. Cot F, McFarland DH. Anatomie-physiologie de la déglutition. In: Cot, F, ed. La dysphagie oropharyngée chez l'adulte. Paris: EDros Inf ServEM;1996:1–28
13. Jean A. Brainstem control of swallowing: neuronal network and cellular mechanisms. Physiol Rev 2001;81:929–969
14. Jean A, Car A, Kessler JP. Brainstem organization of swallowing and its interaction with respiration. In: Miller AD, Bianchi AL, Bishop BP, eds. Neural Control of the Respiratory Muscles. New York: CRC Press; 1997:223–237
15. Martin RE, Goodyear BG, Gati JS, Menon RS. Cerebral cortical representation of automatic and volitional swallowing in humans. J Neurophysiol 2001;85:938–950
16. Sawczuk A, Mosier KM. Neural control of tongue movement with respect to respiration and swallowing. Crit Rev Oral Biol Med 2001;12(1):18–37
17. McFarland DH, Lund JP. Modification of mastication and respiration during swallowing in the adult human. J Neurophysiol 1995b;74:1509–1517
18. Doty RW. Neural organization of deglutition. In: Code CF, ed. Handbook of Physiology. Alimentary Canal, Motility. Washington, DC: American Physiological Society; 1968:1861–1902
19. Von Euler C. Brain stem mechanisms for generation and control of breathing pattern. In: Fishman AP, Cherniak NS, Widdicombe JG, Geiger SR, eds. Handbook of Physiology. Section 3: The Respiratory System. Volume II. Control of Breathing. Bethesda, MD: American Physiological Society; 1986:1–67
20. Bianchi AL, Pasaro R. Organization of central respiratory neurons. In: Miller AD, Bianchi AL, Bishop BP, eds. Neural Control of the Respiratory Muscles. New York: CRC Press; 1997:77–89
21. Charbonneau I, Lund JP, McFarland DH. Breathing and swallowing coordination after laryngectomy. J Speech Lang Hear Res 2005;48: 34–44
22. Gestreau C, Milano S, Bianchi AL, Grelot L. Activity of dorsal respiratory group inspiratory neurons during laryngeal-induced fictive coughing and swallowing in decerebrate cats. Exp Brain Res 1996;108(2):247–256
23. Kessler JP, Jean A. Inhibition of the swallowing reflex by local application of serotonergic agents into the nucleus of the solitary tract. Eur J Pharmacol 1985;118(1–2):77–85
24. Larson CR, Yajima Y, Ko P. Modification in activity of medullary respiratory-related neurons for vocalization and swallowing. J Neurophysiol 1994;71(6):2294–2304
25. Miller AJ. The search for the central swallowing pathway: the quest for clarity. Dysphagia 1993; 8(3):185–194
26. Oku Y, Tanaka I, Ezure K. Activity of bulbar respiratory neurons during fictive coughing and swallowing in the decerebrate cat. J Physiol 1994; 480(Pt 2):309–324
27. Dick TE, Oku Y, Romaniuk JR, Cherniack NS. Interaction between central pattern generators for breathing and swallowing in the cat. J Physiol 1993;465:715–730
28. Kawasaki M, Ogura JH, Takenouchi S. Neurophysiologic observations of normal deglutition. I. Its relationship to the respiratory cycle. Laryngoscope 1964;74:1747–1765
29. McFarland DH, Lund JP. An investigation of the coupling between respiration, mastication, and swallowing in the awake rabbit. J Neurophysiol 1993;69:95–108
30. McFarland DH, Lund JP. The control of speech. In: Cody FWJ, ed. Studies In Physiology—Neural Control of Skilled Human Movement. London: Portland Press; 1995a:61–75
31. McFarland DH, Lund JP, Gagner M. Effects of posture on the coordination of respiration and swallowing. J Neurophysiol 1994;72:2431–2437
32. Palmer JB, Rudin NJ, Lara G, Crompton AW. Coordination of mastication and swallowing. Dysphagia 1992;7(4):187–200
33. Clark GA. Deglutition apnoea. J Physiol 1920;54: LIX–LXI
34. Nishino T, Sugimori K, Kohchi A, Hiraga K. Nasal constant positive airway pressure inhibits the swallowing reflex. Am Rev Respir Dis 1989;140(5): 1290–1293

35. Smith J, Wolkove N, Colacone A, Kreisman H. Coordination of eating, drinking and breathing in adults. Chest 1989;96:578–582
36. Miller AJ. Deglutition. Physiol Rev 1982;62(1): 129–184
37. Ren J, Shaker R, Zamir Z, Dodds WJ, Hogan WJ, Hoffmann RG. Effect of age and bolus variables on the coordination of the glottis and upper esophageal sphincter during swallowing. Am J Gastroenterol 1993;88(5):665–669
38. Shaker R, Dodds WJ, Dantas RO, Hogan WJ, Arndorfer RC. Coordination of deglutitive glottic closure with oropharyngeal swallowing. Gastroenterology 1990;98(6):1478–1484
39. Martin-Harris B, Brodsky MB, Michel Y, Ford CL, Walters B, Heffner J. Breathing and swallowing dynamics across the adult lifespan. Arch Otolaryngol Head Neck Surg 2005b;131:762–770
40. Jacob P, Kahrilas PJ, Logemann JA, Shah V, Ha T. Upper esophageal sphincter opening and modulation during swallowing. Gastroenterology 1989; 97:169–178
41. Logemann JA, Kahrilas PJ, Cheng J, et al. Closure mechanisms of the laryngeal vestibule during swallow. Am J Physiol 1992;262:G338–G344
42. Cook IJ, Dodds WJ, Dantas RO, et al. Timing of videofluoroscopic, manometric events, and bolus transit during the oral and pharyngeal phases of swallowing. Dysphagia 1989;4:8–15
43. Dantas RO, Kern MK, Massey BT, et al. Effect of swallowed bolus variables on oral and pharyngeal phases of swallowing. Am J Physiol 1990; 258(5 Pt 1):G675–G681
44. Hiss SG, Treole K, Stuart A. Effects of age, gender, bolus volume, and trial on swallowing apnea duration and swallow/respiratory phase relationships of normal adults. Dysphagia 2001; 16:128–135
45. Hiss SG, Strauss M, Treole K, Stuart A, Boutilier S. Effects of age, gender bolus volume, bolus viscosity, and gustation on swallowing apnea onset relative to lingual bolus propulsion onset in normal adults. J Speech Lang Hear Res 2004;47:572–583
46. Pouderoux P, Kahrilas PJ. Deglutitive tongue force modulation by volition, volume and viscosity in humans. Gastroenterology 1995;108:1418–1426
47. Castell JA, Dalton CB, Castell DO. Effects of body position and bolus consistency on the manometric parameters and coordination of the upper esophageal sphincter and pharynx. Dysphagia 1990;5(4):179–186
48. Martin-Harris B, Michel Y, Castell DO. Physiologic model of oropharyngeal swallowing revisited. Otolaryngol Head Neck Surg 2005a;133:234–240
49. Robbins J. The evolution of swallowing neuroanatomy and physiology in humans: a practical perspective. Ann Neurol 1999;46(3):279–280
50. Price CJ, Crinion J. The latest on functional imaging studies of aphasic stroke. Curr Opin Neurol 2005;18:429–434
51. Perkell JS, Matthies ML, Svirsky MA. Articulatory evidence for acoustic goals for consonants. J Acoust Soc Am 1994;96:3326
52. Guenther FH. Speech sound acquisition, coarticulation, and rate effects in a neural network model of speech production. Psychol Rev 1995;102:594–621
53. Perkell JS, Matthies ML, Lane H, et al. Speech motor control: acoustic goals, saturation effects, auditory feedback and internal models. Speech Communication 1997;22:227–250
54. McFarland DH, Baum SR, Chabot C. Speech compensation to structural modifications of the oral cavity. J Acoust Soc Am 1996;100:1093–1104
55. Ballard KJ, Robin DA, Folkins JW. An integrative model of speech motor control: a response to Ziegler. Aphasiology 2003;17:37–48
56. Ziegler W. Speech motor control is task-specific. Evidence from dysarthria and apraxia of speech. Aphasiology 2003;17:3–36
57. Kern M, Birn R, Jaradeh S, et al. Swallow-related cerebral cortical activity maps are not specific to deglutition. Am J Physiol Gastrointest Liver Physiol 2001;280(4):G531–G538
58. Mosier K, Bereznaya I. Parallel cortical networks for volitional control of swallowing in humans. Exp Brain Res 2001;140(3):280–289
59. Suzuki M, Asada Y, Ito J, Hayashi K, Inoue H, Kitano H. Activation of cerebellum and basal ganglia on volitional swallowing detected by functional magnetic resonance imaging. Dysphagia 2003;18(2):71–77
60. Martin RE, MacIntosh BJ, Smith RC, et al. Cerebral areas processing swallowing and tongue movement are overlapping but distinct: a functional magnetic resonance imaging study. J Neurophysiol 2004;92(4):2428–2443
61. Zald DH, Pardo JV. The functional neuroanatomy of voluntary swallowing. Ann Neurol 1999;46:281–286
62. Toogood JA, Barr AM, Stevens TK, Gati JS, Menon RS, Martin RE. Discrete functional contributions of cerebral cortical foci in voluntary swallowing: a functional magnetic resonance imaging (fMRI) "Go, No-Go" study. Exp Brain Res 2005;161(1):81–90
63. Satow T, Ikeda A, Yamamoto J, et al. Role of primary sensorimotor cortex and supplementary motor area in volitional swallowing: a movement-related cortical potential study. Am J Physiol Gastrointest Liver Physiol 2004;287(2):G459–G470
64. Bookheimer SY, Zeffiro TA, Blaxton TA, Gaillard PW, Theodore WH. Activation of language cortex

with automatic speech tasks. Neurology 2000; 55(8):1151–1157
65. Riecker A, Ackermann H, Wildgruber D, et al. Articulatory/phonetic sequencing at the level of the anterior perisylvian cortex: a functional magnetic resonance imaging (fMRI) study. Brain Lang 2000;75(2):259–276
66. Saarinen T, Laaksonen H, Parviainen T, Salmelin R. Motor cortex dynamics in visuomotor production of speech and non-speech mouth movements. Cereb Cortex 2006;16(2):212–222
67. Corfield DR, Murphy K, Josephs O, et al. Cortical and subcortical control of tongue movement in humans: a functional neuroimaging study using fMRI. J Appl Physiol 1999;86(5):1468–1477
68. Watanabe J, Sugiura M, Miura N, et al. The human parietal cortex is involved in spatial processing of tongue movement—an fMRI study. Neuroimage 2004;21(4):1289–1299
69. Deiber MP, Ibanez V, Sadato N, Hallett M. Cerebral structures participating in motor preparation in humans: a positron emission tomography study. J Neurophysiol 1996;75(1): 233–247
70. Lee KM, Chang KH, Roh JK. Subregions within the supplementary motor area activated at different stages of movement preparation and execution. Neuroimage 1999;9(1):117–123
71. Kurata K, Tsuji T, Naraki S, Seino M, Abe Y. Activation of the dorsal premotor cortex and presupplementary motor area of humans during an auditory conditional motor task. J Neurophysiol 2000;84(3):1667–1672
72. Binkofski F, Buccino G, Posse S, Seitz RJ, Rizzolatti G, Freund H. A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. Eur J Neurosci 1999;11(9):3276–3286
73. Gerardin E, Sirigu A, Lehericy S, et al. Partially overlapping neural networks for real and imagined hand movements. Cereb Cortex 2000;10(11): 1093–1104
74. Iacoboni M, Woods RP, Brass M, Bekkering H, Mazziotta JC, Rizzolatti G. Cortical mechanisms of human imitation. Science 1999;286(5449): 2526–2528
75. Koski L, Wohlschlager A, Bekkering H, et al. Modulation of motor and premotor activity during imitation of target-directed actions. Cereb Cortex 2002;12(8):847–855
76. Buccino G, Binkofski F, Fink GR, et al. Action observation activates premotor and parietal areas in a somatotopic manner: an fMRI study. Eur J Neurosci 2001;13(2):400–404
77. Ross MG, Nijland MJ. Fetal swallowing: relation to amniotic fluid regulation. Clin Obstet Gynecol 1997;40:352–365
78. Ross MG, Nijland MJ. Development of ingestive behavior. Am J Physiol 1998;274:R879–R893
79. Illingworth RS, Lister J. The critical or sensitive period, with special reference to certain feeding problems in infants and children. J Pediatr 1964; 65:839–848
80. Mayberry RI, Eichen EB. The long-lasting advantage of learning sign language in childhood: Another look at the critical period for language acquisition. J Mem Lang 1991;30:486–512
81. Noterdaeme M, Mildenberger K, Minow F, Amorosa H. Evaluation of neuromotor deficits in children with autism and children with a specific speech and language disorder. Eur Child Adolesc Psychiatry 2002;11:219–225
82. Robbins JA, Hamilton JW, Lof GL, Kempster G. Oropharyngeal swallowing in normal adults of different ages. Gastroenterology 1992;103:823–829
83. Kramer AF, Bherer L, Colcombe SJ, Dong W, Greenough WT. Environmental influences on cognitive and brain plasticity during aging. J Gerontol A Biol Sci Med Sci 2004;59:M940–M957
84. Sawaki L, Yaseen Z, Kopylev L, Cohen LG. Age-dependent changes in the ability to encode a novel elementary motor memory. Ann Neurol 2003;53: 521–524
85. Bwielamowicz S, Gupta A, Sekhar LN. Early arytenoid adduction for vagal paralysis after skull base surgery. Laryngoscope 2000;110:346–351
86. Cornwell PL, Murdoch BE, Ward EC, Morgan A. Dysarthria and dysphagia as long-term sequelae in a child treated for posterior fossa tumour. Pediatr Rehabil 2003;6:67–75
87. Dworkin JP, Hartman DE. Progressive speech deterioration in dysphagia in amyotrophic lateral sclerosis: case report. Arch Phys Med Rehabil 1979;60:423–425
88. Muller J, Wenning GK, Verny M, et al. Litvan I. Progression of dysarthria and dysphagia in post-mortem-confirmed parkinsonian disorders. Arch Neurol 2001;58:259–264
89. Nishio M, Niimi S. Relationship between speech and swallowing disorders in patients with neuromuscular disease. Folia Phoniatr Logop 2004; 56: 291–304
90. Litvan I, Sastry N, Sonies BC. Characterizing swallowing abnormalities in progressive supranuclear palsy. Neurology 1997;48:1654–1662
91. Martin BJW, Corlew MM. The incidence of communication disorders in dysphagic patients. J Speech Hear Disord 1990;55:28–32

92. Burres S. Intralingual injection of particulate fascia for tongue paralysis. Laryngoscope 2004;114:1204–1205
93. El-Sharkawi A, Ramig L, Logemann J, et al. Swallowing and voice effects of Lee Silverman Voice Treatment: a pilot study. J Neurol Neurosurg Psychiatry 2002;72:31–36
94. Farley BG, Koshland GF. Training BIG to move faster: the application of the speed-amplitude relation as a rehabilitation strategy for people with Parkinson's disease. Exp Brain Res 2005;167:462–467
95. Farley BG, Koshland GF. Learning Big: efficacy of a large-amplitude exercise approach for patients with Parkinson's disease—bradykinesia to balance. Mov Disord 2005b;20(10):S137
96. Fox CM, Farley BG, Ramig LO, McFarland D. An integrated rehabilitation approach to Parkinson's disease: learning big and loud. Mov Disord 2005;20(10):S127