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**Coordinator’s Column**

Lynn Marty Grames

In August of 2008, the Division 5 Steering Committee (SC) met at the ASHA National Office (NO) to develop a 3-year Strategic Plan for the division. The draft plan was reworked during the fall and finalized in November 2008. The completed version will appear on our Division page of the ASHA Web site: http://www.asha.org/members/divs/div_5.htm. As I review the plan now, it seems that a great deal has changed in a very short time. Some of the plan already seems antiquated, or at least items that seemed high priority 11 months ago seem much less urgent now. What has happened in the meantime?

Economic collapse happened. The effects of the troubled economy have flowed into the Association’s Division functions as they have flowed into our training programs, clinical programs, and research programs. Reduced income from interest and an increase in expenses have reduced our bottom line. Consequently, the Association is asking all programs, including the Division program, to identify ways to reduce expenses; opportunities to generate income are limited. The SC is evaluating expense reductions in Short Course arrangements, face-to-face meetings, and “extra” expenses.

As in the Association, corporate America has had to evaluate programs and reduce expenses. Allyn & Bacon Publishers, long-time sponsor of the Willard R. Zemlin Memorial Lecture in Speech Science, discontinued its sponsorship. The SC is considering various options concerning the Zemlin Lecture as this issue goes to press.

Many political observers now agree that health care reform will be a cornerstone of the Obama administration’s legislative agenda, and stakeholders are gearing up for advocacy during this process. If passed by Congress, health care reform will likely touch a great many of our affiliates through their institutions, the patients for whom they provide services, and the third-party payers with whom they must do business. Effects on affiliates will certainly in turn affect the Division.

We have always felt that increasing the amount of education in the speech and hearing sciences and in orofacial disorders will advance the profession at large, but advocating for change at the academic level seems less politically correct while some training programs are fighting for survival. It will fall to us, as Division affiliates, to provide continuing education to our colleagues in speech science and orofacial disorders as much as we can, until the economic situation does not threaten the existence of some of our training programs.

In what other ways will our future plans be altered? Shrinking division reserves mean that we will need to be open to other sources of revenue. If affiliate fees are our primary revenue source, we will need to increase our affiliate numbers. This is a challenge when Special Interest Division affiliation may be considered a luxury that might be readily trimmed at the next membership renewal. We need to be certain that Division affiliation has a value that professionals cannot do without, and we will need to find ways of providing value to potential members: students and newly minted professionals alike.

Continuing education programs and products are alternate sources of revenue for the divisions. We have conducted a symposium for the past 3 years in conjunction with the
American Cleft Palate-Craniofacial Association directed toward the community clinician caring for the child with a cleft palate. This has been a break-even event for the most part.

A strategic plan is a valuable document; it maps a course for our Division, while at the same time provides an accountability yardstick for the Division to the larger Association, and for the SC to its affiliates. However, it needs to also be fluid in order to accommodate changes in the economic, educational, and professional climate. We need every affiliate to recruit colleagues and to offer creative solutions to the challenges posed by our current economic climate. Please offer your ideas and suggestions, to the SC, via the e-mail list, or through the discussion forum.
The views expressed are those of the author and do not reflect the views of Division 5 or the Association.

**Editor’s Column**

Richard D. Andreatta

**Interesting Times**

To paraphrase a Chinese proverb... we are truly living in interesting times. Since our last issue in 2008, we have been witness to many landmark events in the history of this Nation, from the election of our country’s first African-American President to the emergence of an unprecedented economic crisis. From the perspective of science, these events have, in subtle and not so subtle ways, altered the landscape for those of us working in the basic and clinical science-based fields. The most dramatic change, albeit mostly psychological at this point in time, is the clear shift from an administration that had an adversarial relation with and aversion to the sciences, to one that embraces the sciences as a catalyst for change and views science as a critical partner for the future growth and prosperity of our country. It has been encouraging to hear from President Obama in the context of very high profile speeches, the prominent role that science will have at the table in shaping his administration’s energy, health, and economic policies.

The second dramatic change that has affected every sector of our society has been the profound downturn of the economy. Our Nation’s state-funded academic institutions are struggling to make ends meet, seeing their budgets reduced, faculty furloughed, and support staff laid off. While most of the economic news is depressing to follow day in and day out, the financial downturn has had some interestingly positive effects on the business of science. The recently passed stimulus package has delivered a large bolus of funding into major research gatekeepers, such as the National Institutes of Health and the National Science Foundation. While much of the stimulus windfall is geared toward institution-based infrastructure and projects that can have immediate effects on job creation, the trend that it portends for the future is for the reversal of the funding stagnation evidenced during the last 8 years.

The economic impact of investments in research and science has been shown time and time again to reap huge dividends for every dollar spent. These dividends are realized directly in terms of job growth, product development, health care advances, and a general progression of our quality of life. Clearly, we are in a state of flux politically as the new administration works to reverse the disturbing anti-intellectual attitudes fostered by the previous administration. We are also continuing to face much uncertainty economically in our near future, with difficult times still ahead. Yet, as we move forward, let’s not forget Albert Einstein’s now famous statement that “in the middle of difficulty lies opportunity.” I believe that the scientific disciplines have a once-in-a-generation opportunity to prove their worth to society and solidify their place as the “go to” people to solve our national and global problems. To secure this future and our place at the table, we must all actively contribute to public advocacy for the science performed in our respective areas. Advocacy to our communities, our representatives at both state and federal levels, and our professionally related colleagues is crucial for the long-term health and continued growth of our common commitment to discovery. If everyone were to give simply 1 hour a month toward some advocacy-related activity... just imagine what we could accomplish for the betterment of those we serve.
Talking a Look Inside

In this issue, we continue an important tradition of providing you with a written summary of the past year’s winner of the Zemlin Memorial Award, an award given to a person whose impact on speech science has been profound and groundbreaking. This past year’s winner was Dr. Charles (Chuck) Larson. Dr. Larson’s lecture at the 2008 ASHA annual Convention provided a detailed summary of his lab’s work and efforts during the past 15 years. In his article for Perspectives, Dr. Larson summarizes a series of novel studies that were designed to learn if auditory feedback of one’s voice is used in real-time to make corrections for errors in F0 production. These studies have revealed that the monitoring of one’s acoustic output can provide critical feedback information to sensorimotor regions of the brain regulating laryngeal behavior.

The remainder of this issue highlights the research output of one of the most productive and innovative lab groups working in the speech sciences, the Communication Neuroscience Laboratories at the University of Kansas, directed by Dr. Steven M. Barlow. Dr. Barlow’s lab group has written a series of papers for this issue highlighting both the basic and clinical aspects of their orofacial-related research agenda. These are fascinating papers covering a wide range of topics from the creation of novel instrumentation to assess speech subsystems, to the application of neuroscience principles to pro-habilitate pre-term infants lacking the capacity to generate appropriate suck behavior. My hope is that these papers will provide you with an overview of one of this country’s premier research groups studying orofacial systems.

Last, and on a rather sad note, Dr. Thomas Hixon of the University of Arizona died unexpectedly this past spring, leaving his family, friends, and colleagues shocked and deeply saddened. Dr. Hixon was a pioneer in the investigation of respiratory dynamics during speech and song and was recently honored by Division 5 as the 2005 recipient of the Zemlin Award in Speech Science. His works have become foundational components of our literature, and his legacy of excellence and rigor through his numerous books and journal articles are a valuable gift that we can all look to for guidance in his absence. He was a friend and mentor to countless students and working professionals in the field. I will always remember his brilliant 2005 Zemlin award lecture at ASHA, as well as his uncompromising scientific mind and ethics. The field of speech science is diminished by Dr. Hixon’s untimely departure from this world. He will be truly missed.
2008 Zemlin Award in Speech Sciences Memorial Lecture:
The Role of Auditory Feedback for the Control of Voice
Fundamental Frequency and Amplitude

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Abstract

Previous research has failed to identify precise neural mechanisms involved in auditory feedback regulation of vocalization. The goal of this research project was to improve our understanding of neural mechanisms controlling the voice. Participants were instructed to sustain a vowel or repeat phrases during which perturbations in voice pitch or loudness feedback were presented. Voice signal averaging, neuroimaging, laryngeal electromyography, and cortical event-related potential techniques were used to measure vocal and neural responses to perturbed feedback. Pitch- and loudness-shifted voice feedback triggers small automatic corrective responses in voice fundamental frequency and amplitude during vowel or speech production. Larger responses during speech suggest task modulation of these responses. Larger responses were also recorded in individuals with Parkinson’s disease and children with autism than in normal controls. Neural recording techniques revealed cortical activation during these responses. Cortical mechanisms are involved in generating corrective vocal responses to perturbations in voice auditory feedback. This system helps control the voice during speech and dynamically adjusts responses to meet vocal goals. Abnormally large responses in individuals with Parkinson’s disease and autism suggest that the audio-vocal mechanisms just described may be involved in the speech and vocalizations of these individuals as well.

Introduction

This article summarizes a series of studies completed over the past 14 years that were designed to determine whether auditory feedback of one's voice is used online to make corrections for errors in production. Before these studies, Elman (1981) had shown that when speakers were presented with pitch-shifted voice feedback, they changed their voice fundamental frequency ($F_0$). However, neither the timing of the responses nor their magnitudes were reported, which precluded meaningful interpretation of the data in regard to the goal of the present experiments. Our studies began by defining the nature of vocal responses to pitch-shifted voice feedback and the optimal stimulus parameters for eliciting these responses. Later studies addressed the question of whether or not the nature of the vocal task (e.g., speaking) could modulate responses to pitch-shifted feedback. Our most recent studies are examining the neural and neuromuscular mechanisms underlying these responses.
**Methodology**

Most of our studies have involved normal young adult participants, although in recent years we have also done studies on people with voice disorders. Briefly, participants are instructed to vocalize a vowel or else speak a phrase while they listen to their voice over headphones. We introduce brief (200 to 1,000 ms) perturbations in their voice pitch or loudness feedback with the use of an Eventide harmonizer (Ultra harmonizer or Eclipse). The participant’s voice and the signal going into the headphones are recorded for later analysis. We analyze the vocal responses to pitch- or loudness-shifted stimuli by averaging the voice F₀ or amplitude trajectory over the course of approximately 20 trials. Measures of responses are taken from the averages of the voice F₀ or amplitude signal.

**Results**

In our first major study (Burnett, Freedland, Larson, & Hain, 1998), we tested the effects of voice loudness, added masking noise, pitch-shift stimulus magnitude, pitch-shift direction, and pitch-shift duration. One of the most important observations we made was that responses generally opposed the direction of the pitch-shift stimulus; that is, an upward pitch-shift stimulus (increase in pitch of the voice) led to a downward F₀ response (see Figure 1). Such compensatory responses are common in various stimulus-response behaviors and are generally thought to have a stabilizing influence on the system. In the present case, vocal compensatory responses were suggested to operate as a negative feedback system to help stabilize voice F₀ around a desired target. Despite such responses, about 10-15% of responses changed in the same direction as the stimulus (termed “following” responses), and we are still attempting to learn what causes them. Both types of responses have a latency of 100-150 ms. This latency, coupled with the fact that they are directionally sensitive, led to the suggestion that the responses were automatic.

*Figure 1. Graphical displays of averaged voice F₀ traces in response to control and perturbation trials. Top graph (red) shows average voice F₀ trajectory to an upward pitch-shift stimulus (square bracket below) and average trajectory to control (no-stimulus) trials. Vertical bars represent standard error of the mean of all responses. Bottom graph shows average F₀ trajectory (blue) to downward pitch-shift stimulus and to control trials.*

It was also found that the response magnitudes were relatively constant across stimulus magnitudes of 50 to 300 cents (100 cents = 1 semitone or ½ step). As a result, it was
deemed doubtful that such responses could exert a major effect on voice F₀ control, thus leaving large changes in F₀ to be controlled voluntarily. Also, voice loudness or the presence of masking noise had little effect on the responses. This important observation suggested that absolute stimulus and environmental controls were not critical to the conduct of experiments of this type. Thus, patients could be easily tested in a clinic or hospital room without major negative effects on the responses. Indeed, in studies on individuals with Parkinson's disease (PD) and the study on children with autism, testing was conducted in a clinical treatment room or office.

When we extended the duration of the pitch-shift stimuli from 25 ms to 300 ms, it was found that response magnitudes and durations progressively increased. With the longest duration stimuli, two distinct peaks in average responses were noted (Figure 2). This observation prompted a second experiment in which we attempted to separate the two peaks by instructing the participants to make voluntary responses to pitch-shift stimuli (Hain et al., 2000). Specifically, in one case participants were instructed to ignore the pitch-shift stimulus, in another case to change their voice F₀ in the direction opposite to the stimulus, and in a third case to change their F₀ in the same direction as the stimulus (stimulus durations were 1 second long). The latter two instructions led to the finding that the first response generally opposed the direction of the stimulus regardless of the instruction, whereas the second response followed the instructions. Thus, this experiment showed that long-duration stimuli can elicit an early reflexive and a later voluntary response. In the context of speaking or singing, an unplanned change in voice F₀ would lead to a rapid but small response to correct for the error, and if the reflex was unsuccessful in correcting for the error, a later voluntary response by the speaker would adjust F₀ to the desired level.

**Figure 2.** Averaged voice F₀ trajectories to downward (left) and upward (right) pitch-shift stimuli of different durations. Duration of stimuli is indicated by numbers on the left. Vertical dashed line indicates time of stimulus onset. Arrows point to instances of double peaks (see text). Reprinted with permission from Burnett, T. A., Freedland, M. B., Larson, C. R., & Hain, T. C., *Journal of the Acoustical Society of America*, 103(6), 3015–3061, 1998. Copyright 1998, Acoustical Society of America.

Because F₀ is just one regulated variable of vocalization, we sought to learn whether voice amplitude was similarly controlled (Bauer, Mittal, Larson, & Hain, 2006). This question was also inspired by the well-known Lombard and side-tone amplification effects (Lane & Tranel, 1971; Lombard, 1911). Using methodology similar to the pitch-shift studies, we presented brief, unexpected changes in voice loudness to vocalizing participants. We observed that most responses were compensatory, had latencies of 100–150 ms, and were rather small in magnitude (i.e., 1 dB or less; Figure 3). These data showed that voice F₀ and amplitude were controlled by very similar mechanisms.
A natural question that followed was whether there was a single system controlling both voice $F_0$ and amplitude or two separate systems. We designed an experiment to address this question (Larson, Sun, & Hain, 2007). Vocalizing participants were presented with (a) pitch-shift stimuli alone; (b) loudness-shift stimuli alone; (c) pitch- and loudness-shift stimuli at the same time, both changing in the same direction (both up or both down); and (d) pitch- and loudness-shift stimuli, both changing at the same time in opposite directions (pitch up and loudness down, or vice versa; Figure 4). The most interesting data were from the same-direction or opposite-direction conditions, where it was found that an $F_0$ and amplitude response could occur at the same time and that both could be in the same or opposite directions (Figure 5). These results did not answer the question of whether or not there is one or two separate systems, but they did show that the audio-vocal system can generate $F_0$ and amplitude responses simultaneously and independent of one another. It is not surprising that the auditory system can hear simultaneous changes in frequency and loudness, but it is quite remarkable that the perceptual-motor system can then automatically produce independent responses in each domain.

Figure 4. Schematic illustration of experimental conditions when either voice pitch- or loudness-shift stimulus occurred or where both pitch and loudness were perturbed either in the same or different directions. Stimulus magnitudes were $\pm 50$ cents and $\pm 3$ dB. Reprinted with permission from Larson, C. R., Sun, J., & Hain, T. C., Journal of the Acoustical Society of America, 121(5), 2862–2872, 2007. Copyright 2007, Acoustical Society of America.
**Figure 5.** Averaged voice F0 response (blue) or amplitude response (red) to simultaneously presented pitch- and loudness-shift stimuli.

**Responses to Perturbed Auditory Feedback**

An important issue related to most studies of reflexes has to do with the extent to which they may be modified by task parameters and performance. Such task dependency would help in our understanding of complex neural mechanisms regarding many types of behavior. For example, showing that the pitch-shift reflex is modified by speech (as we sought to show) would help to understand how auditory feedback is generally used to assist in the control of speech. In our first study, we studied responses to pitch-shifted feedback while Mandarin speakers were repeating nonsense phrases (Xu, Larson, Bauer, & Hain, 2004). Because Mandarin is a tonal language, it was hypothesized that Mandarin speakers would control voice F0 more tightly than speakers of nontonal languages and perhaps rely on auditory feedback to a greater extent to do so (Figure 6).

**Figure 6.** Voice F0 traces during the production of Mandarin syllables (ma ma) in the high tone. Blue curves show response to perturbation and yellow to control trials. Stimulus direction and timing are indicated below each set of traces. Difference waves below show the magnitude of the responses when expressed as the difference between the mean of the average and the mean of the control trials.

We found that Mandarin speakers produced larger responses with shorter latencies than we had previously recorded when participants were sustaining vowel sounds. Moreover,
the fact that the latencies of these responses (100–150 ms) could occur within the same syllable as the stimulus meant that speakers could correct for an error in production fast enough to help affect the meaning of the intended speech goal.

A more explicit test of speech modification of responses to pitch-shifted feedback was done in a study of English speakers (Chen, Liu, Xu, & Larson, 2007). Although English is a nonontonal language, voice F0 is modulated to impart prosody to speech. In a group of English speakers, we found that responses to pitch-shifted feedback stimuli presented just before a planned increase in F0 as part of a question were larger than those the same speakers produced while sustaining vowel sounds (Figure 7). Thus, by showing that the pitch-shift reflex could be modulated during speech of a tonal and nonontonal language, we demonstrated that auditory feedback can be used to help control segmental and suprasegmental sounds of speech in normal speakers.

![Figure 7. Voice F0 trajectories to downward pitch-shift stimuli (left) and upward stimuli (right). Responses to perturbations are in blue and control trials in red. Top traces show F0 trajectories during the phrase “you know Nina?” Bottom traces show responses during steady vowel production. Horizontal dashed lines indicate time of the response.](image)

**Voice Disorders**

There are several types of voice disorders, and a natural question is whether or not abnormal functioning of audio-vocal reflexes may contribute to these disorders. In our first study along these lines, we measured responses to pitch-shifted voice feedback in a group of patients with PD and compared the responses with those from a group of age- and sex-matched control participants (Kirwan & Larson, 2001). Although the PD patients had a mild form of the disease and were on medication during testing, they showed a delay in producing responses relative to control participants. This finding agrees with previous studies (Lee & Tatton, 1975) that have showed that PD patients sometimes produce abnormal responses to sensory feedback.

More recently, we compared responses in PD patients and controls to both pitch- and loudness-shifted voice feedback. This group of PD patients had a more severe form of the disease and had been off of medication for 12 hours before testing. We found that the PD patients had larger response magnitudes to both types of feedback than did the controls. Because it is well known that PD patients tend to talk too quietly, it can be speculated that the reason for our patients’ abnormal voice control was that their voice feedback seems too loud to them, and they therefore attempt to talk more quietly.

We also tested a group of children with autism on pitch-shifted voice feedback (Russo, Larson, & Kraus, 2008). Autistic children are known in some cases to have abnormal speech prosody and social affect. We hypothesized that they would show abnormal responses to perturbed auditory feedback. Several of the children produced responses that were larger than the responses of control children, and others produced responses that had smaller magnitudes than those of the controls. The autistic children demonstrated deficits in language testing as
well. These results, as do those of the PD patients, demonstrate that some groups of people with neurological or behaviorally linked voice disorders also respond abnormally to perturbed auditory feedback. These findings need to be replicated in both of these populations as well as in patients with other types of voice disorders. This type of testing may be of importance in diagnosing the cause of some types of voice disorders.

**Neuromuscular Mechanisms of the Audio-Vocal System**

There is a great deal of evidence to support the view that intrinsic laryngeal muscles control voice $F_0$ (Hirano & Ohala, 1969; Hirano, Vennard, & Ohala, 1970; Larson, Kempster, & Kistler, 1987; Luschei, Ramig, Baker, & Smith, 1999; Luschei, Ramig, Finnegan, Baker, & Smith, 2006). We therefore hypothesized that both the cricothyroid (CT) and thyroarytenoid (TA) muscles would be involved in responses to pitch-shifted voice feedback (Figure 8). We implanted hooked-wire, stainless steel wires (0.002 inches) into the CT and TA muscles and recorded electromyograms (EMGs) along with the vocal signal while the subjects sustained a vowel sound and received pitch-shifted voice feedback. Both the CT and TA muscles responded to decreases in pitch feedback with an increase in activity beginning at 50 to 60 ms after the stimulus (Larson, Liu, Behroozmand, & Bove, 2008). The same muscles showed a decrease in activity with the same latency in response to an increase in voice pitch feedback. These results provide important evidence on the muscles that are involved in these responses and indicate the speed with which the nervous system can activate the muscles to generate the vocal responses.

![Figure 8](image)

*Figure 8. Average voice $F_0$ trajectories (top, red), pitch-shift stimuli (black), combined left and right TA EMG, and combined left and right CT EMG traces (blue, bottom). Note the resemblance of changes in $F_0$ trajectory to the average CT EMG trace.*

In our most recent research, we have begun direct studies of neural activity related to the audio-vocal system. In one set of studies, we are recording event-related potentials from scalp electrodes while vocalizing participants receive pitch-shifted feedback (Behroozmand, Karvelis, Liu, & Larson, 2009). One theoretical issue that has received significant research interest in recent years is the suppression of auditory cortex activity during vocalization. Several studies have demonstrated that, during vocalization, auditory cortex potentials are smaller in magnitude than recording potentials while participants listen to the playback of their vocalization. We sought to determine whether responses to pitch-shifted voice feedback were also suppressed. Twenty participants were tested in a paradigm in which neural potentials were recorded from 13 different electrodes positioned over the frontal and temporal cortex 1 (0–20 international system) while participants vocalized and received pitch-shifted voice feedback. After recording of potentials while participants were vocalizing, participants quietly listened to the playback of pitch-shifted voice recording (Figure 9).
Results showed that the cortical responses were larger for the vocalizing condition than for the listening condition (Figure 10). These findings indicated that the neural responses to pitch-shifted voice auditory feedback were larger than those during quiet listening. This seemingly contradictory finding is explained by a recent study with monkeys in which single neurons were recorded during vocalization (Eliades & Wang, 2008). There it was found that whereas some neurons were suppressed with vocalization, others were excited. Moreover, the suppressed neurons had a greater dynamic range for responding to changes in voice auditory feedback. Thus, an interpretation of our data is that, during vocalization, the auditory cortex is in fact primed to be more sensitive to changes in voice feedback. The reason for this behavior may be that by being more sensitive to one’s own voice, the system has a greater capability to monitor and correct for errors in production. There is still suppression of the auditory cortex for the onset of vocalization, but at the same time the auditory cortex may be more sensitive to one’s own voice than another person’s.
Figure 10. Structural fMRI image of the brain of a patient suffering from epilepsy. Colored rectangles indicate surface area covered by electrode grids. Coloration is applied to grids to indicate average electrical activity from electrodes distributed throughout grids. Red area in top grid indicates activation of laryngeal motor cortex at 30 ms after pitch-shift stimulus.

In another series of studies, we are recording neural potentials directly from the surface of the brain (electrocorticography) in epilepsy patients. These studies were done in conjunction with Dr. Matthew Howard and Dr. Jeremy Greenlee from the Department of Neurosurgery at the University of Iowa. In these studies, patients with intractable epilepsy are surgically prepared for direct recording from the cortical surface with grids of electrodes, which are used to monitor brain activity and thereby detect and locate sites of generation for seizures. During the 2-week period in which the patients are monitored in the hospital, they consent to participate in a variety of studies. In our case, the patients were asked to vocalize or to speak phrases while receiving pitch-shifted or delayed auditory feedback. In the first patients from whom we have recorded, we have found that the laryngeal area of the motor cortex in the right hemisphere is excited about 30–40 ms after a pitch-shift stimulus (Figure 11). Slightly later, a potential is also recorded in the inferior frontal gyrus (IFG). At about 60–65 ms, widespread potentials are recorded in the superior temporal gyrus. When the patients then quietly listened to the recorded playback of their vocalizations, motor cortex and IFG potentials were not observed. These potentials were also not recorded in the left hemisphere. However, both hemispheres demonstrated a great deal of activity in the auditory cortex beginning about 65 ms after onset of the playback vocalizations. Thus, these studies are able to provide us with detailed information on the timing and location of neural activity involved in responding to pitch-shifted voice feedback.
Figure 11. Averaged voice F0 trajectories after pitch-shift stimuli (Time 0), followed by TMS pulse at delay times indicated on the right. Top thick trace shows F0 trace after pitch-shift stimulus without TMS pulse. Pitch-shift direction is indicated at bottom. Circled potentials resulting from TMS pulses were measured across three different levels of TMS pulse magnitudes. TMS intensity is expressed as a percentage (117%) of threshold for a response in the first dorsal interosseous muscle from stimulation of the hand area of the motor cortex (MEP).

An additional technique we are using to study brain mechanisms involved in these reflexes is a combination of functional magnetic resonance imaging (fMRI) and transcranial magnetic stimulation (TMS). These studies are being done at the Research Imaging Center of the University of Texas Health Science Center in San Antonio. Collaborators include Don Robin, Jack Lancaster, and Peter Fox. The goal of the studies is to define the neural circuitry involved in these audio-vocal reflexes. The first step is to obtain fMRI images of the brain during pitch-shifted voice feedback. We use a sparse-sampling protocol to image the brain while participants are vocalizing and receiving pitch-shifted voice feedback. We also use fMRI techniques to acquire a structural image of the brain. We overlay the regions of the brain that were active during pitch-shifted feedback on the structural image. The coordinates of the brain registering this activity are then sent to a robotically controlled TMS system.

In the next phase of the procedures, hooked-wire electrodes are first inserted into the cricothyroid muscle. The participant then lies supine on a table, and the coordinates of the brain activation areas are used to position the TMS coil over the desired area of the brain (e.g., laryngeal motor cortex). The TMS is programmed to deliver pulses to the brain while the participant is vocalizing. Monitoring of laryngeal EMG is used to help verify the correct placement of the coil. Then the participant vocalizes and receives pitch-shifted voice feedback. The TMS system delivers pulses to the brain at specific intervals after pitch-shifted voice feedback (0, 10, 20, 30, 40, 50, and 60 ms). The TMS pulses cause an initial increase in voice F0 followed by a decrease. After the experiment, for each pitch-shift/TMS interval condition, the average magnitude of the initial increase in the F0 is measured (Figure 12). When we use an upward pitch-shift stimulus, we observe a reduction in the F0 response with TMS/F0 intervals of 30–40 ms. The reduction in the F0 measurement is due to the interaction between the TMS pulse and the reduced corticidal activity resulting from the upward pitch-shift stimulus (upward stimuli normally cause a reduction in laryngeal EMG and voice F0). This interval corresponds with the laryngeal motor cortex activation we recorded directly from the brain in epilepsy patients.
Summary

Over the past 14 years, we have made considerable progress in understanding the mechanisms used by people to help regulate their voice $F_0$ and amplitude during vocalization and speech. We have found that a perturbation in voice $F_0$ or loudness feedback causes a compensatory change in voice $F_0$ or amplitude. The compensatory nature of these responses suggests that they function as a negative feedback control system to help regulate the voice. The fact that these responses are rather small in comparison with the range of $F_0$ and amplitude that a person is capable of producing suggests that this system is optimal for stabilizing the voice for small fluctuations, leaving larger fluctuations to be controlled by voluntary mechanisms. By showing that these vocal responses are larger in certain individuals with voice disorders, the data also implicate these regulatory voice mechanisms in some types of voice disorders.

In addition, these results point to the need for further research on individuals with voice disorders. In our most recent studies, we are using a variety of techniques for studying the brain mechanisms underlying such responses. Using event-related potentials, fMRI, electrocorticography, and TMS techniques, we have shown that the laryngeal motor cortex and auditory cortex are involved in these responses. Using these and additional techniques, we hope in the near future to develop a more complete understanding of the neural mechanisms involved in the control of the voice on the basis of auditory feedback.

Acknowledgments

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References


The Communication Neuroscience Laboratories at the University of Kansas: An Overview

Steven M. Barlow

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Abstract

The Communication Neuroscience Laboratories (CNL) celebrates its 25th anniversary in 2009 with a brief overview of past and current research projects concerned with the sensorimotor development and control of orofacial and laryngeal systems subserving speech, vocalization, suck, oromotor, and aeroingestive behaviors in health and disease across the human life span. A key ingredient in the multidimensional study lines described in this review is the assembly and nurturing of a strong multidisciplinary research team involving students and research faculty from communication sciences, biology, neuroscience, bioengineering, computer science, neurology, radiology and medical physics, neonatology, nursing, pediatrics, and physical therapy. The transfer of technology from bench to bedside (or even cribside) is another important function. An example of an innovation from the CNL is highlighted by a new therapeutic sensorimotor entrainment intervention (NTrainer) that helps premature infants with feeding disorders develop ororhythmic (suck) skills. When possible, project lines are directed toward patient-oriented research and innovative interventions aimed at driving mechanisms of brain plasticity to improve communication/oromotor function, neurodevelopmental outcomes, or both.

Origins and Pathways

The origin of the Communication Neuroscience Laboratories (CNL) can be traced to Boys Town National Institute in 1984, when I was recruited to join the institute’s research faculty. Sensorimotor physiology of trigeminofacial systems in animal and human models constituted the principal study line funded by the National Institutes of Health (NIH) through 1990 and resulted in the evolution of new applications to assess facial sensitivity (Barlow, 1987), perioral reflex modulation during motor control (Barlow, 1988, 1991; Barlow & Creutz, 1988), and orofacial force dynamics (Barlow & Abbs, 1986; Barlow & Burton, 1990).

Experiments supported by an NIH program project grant were conducted in collaboration with Boys Town National Institute scientists such as Dr. Glenn Farley, to map the feline brainstem vagal systems during conditioned vocalization (Farley, Barlow, & Netsell, 1992; Farley, Barlow, Netsell, & Chmelka, 1992), and with Dr. Kevin Spangler, to understand the mechanoreceptor properties of the lips with respect to mechanical shear. In addition, response properties of the ventroposteromedial nucleus of the thalamus and primary somatosensory cortex (S1) in the cat (Barlow & Spangler, 1985) were pursued to enhance our understanding of parallel studies in humans.
In January 1990, the CNL was moved to Indiana University in Bloomington. Studies of orofacial somatosensory psychophysics and sensorimotor integration expanded with support from NIH to include normal and disordered systems under a wider range of task dynamics. In part on the basis of the knowledge gained from these experiments, a new study line was developed to investigate trigeminofacial function and ororhythmic pattern generation in infants during the first year of life. This research line quickly led to studies in preterm infants at significant risk for oromotor dysfunction and feeding problems, neurologic insult, and poor neurodevelopmental outcomes. Pursuit of these studies required a significant investment in engineering and technology development to bring servo-controlled stimulation methods and real-time digitally based measurement systems crib side within the challenging environment posed by the neonatal intensive care unit (NICU).

In 2000, the CNL was relocated to its current location at the University of Kansas and expanded to include dedicated facilities for bioengineering, biomechanics, and electrophysiology. Several off-site recording laboratories have also been established to support (a) oromotor developmental studies, (b) motor control effects of deep brain stimulation in Parkinson's disease, and (c) the incorporation of brain imaging methods into our experiments. NIH support for studies of sensorimotor development in the premature infant increased, and a new multi-institutional NIH project line (principal investigator: C. A. Trotman, University of North Carolina; co-investigator: S. M. Barlow, University of Kansas) was initiated to examine facial animation, force dynamics, sensory physiology, and motor control in children undergoing lip revision surgery associated with cleft lip/palate.

**Overview of Current Research**

**Sensorimotor Control and Development in the Orofacial System**

*Relationships among suck central pattern generators (sCPG), oral feed, and neurodevelopmental outcomes.* Suck is a precocial oromotor behavior in humans and is integral to competent oral feeds. However, premature infants often demonstrate oromotor dysooordination and are unable to transition safely to oral feeds. This represents a frequent and serious challenge to both NICU survivors and physician-provider-parent teams. The potential causes of delayed or impaired suck development are numerous and may result from neurological insult to the developing brain, feeding intolerance, postsurgical recovery, diabetes, or lung disease that requires ventilator interventions that interfere with normal ororhythmic pattern formation. For example, lengthy oxygen supplementation procedures in the NICU cost the preterm infant precious sensory and motor experiences during a critical period of brain development when the central patterning of suck and prefeeding skills is being refined. Even the presence of a nasogastric feeding tube has negative effects on sucking and breathing (Shiao, Youngblut, Anderson, DiFiore, & Martin, 1995). Trussing the lower face with poly tubes and tape also restricts the range and types of oral movements available and limits cutaneous experiences with the hand and fingers. Interruption of these experiences may impair fragile syntheses of how the brain maps these functions (Bosma, 1970; Hensch, 2004).

For some preterm infants, poor suck and oromotor dysooordination persist well into early childhood and may lead to significant delays in the emergence of other oromotor behaviors including feeding, babbling, and speech-language production (Adams-Chapman, 2006; Ballantyne, Frisk, & Green, 2006). Moreover, failure to establish oral feeding skills in the NICU may result in the infant being sent home on gavage or G-tube feedings and hinder the development of coordinated oromotor behavior. The difficulties associated with establishing oral feed competence along with the additional costs of extended hospitalization underscore the need for assessment and therapeutic tools to facilitate the development of normal oral motor skills (Barlow, 2009a, 2009b; da Costa, van den Engel-Hoek, & Bos, 2008; Fucile, Gisel, & Lau, 2002, 2005; Lau, 2006).
Fortunately for the human infant, brainstem sCPG responds well to peripheral input (Barlow, Finan, Chu, & Lee, 2008; Finan & Barlow, 1998; Poore, Zimmerman, Barlow, Wang, & Gu, 2008; Rocha, Moreira, Pimenta, Ramos, & Lucena, 2007) and adapts to changes in the local oral environment (Zimmerman & Barlow, 2008). Collective results from NICU studies demonstrate the potent effects of a motorized silicone pacifier nipple on the development of nonnutritive suck (NNS) in preterm infants. The patterned orocutaneous experience is physiologically salient and spectrally patterned to resemble the “burst-pause” structure of the NNS. This form of stimulation serves to entrain the activity patterns of vast populations of mecanoreceptor afferents located in the lips, tongue, and jaw of the neonate, which in turn influence firing patterns of the respective orofacial lower motor neurons. This is a central tenet of one of the basic principles of neural pathway formation: “Neurons that fire together will wire together” (Löwel & Singer, 1992).

**Patterned orocutaneous entrainment: A new intervention during late gestation among premature infants in the neonatal intensive care unit.** The application of mechanosensory entrainment as a habilitation strategy has ecological validity in assisting the infant to produce appropriate oromotor output. This approach is consistent with contemporary ideas on the role of sensory-driven neural activity in pathway formation (Marder & Rehm, 2005; Penn & Shatz, 1999) and the notion that appropriate oral experiences may be critical in the final weeks of gestation for the formation of functional central neural circuits. The richness of the patterned orocutaneous experience offered by the NTrainer technology developed in our laboratory (described subsequently) presents a new neurotherapeutic application for the habilitation of suck in premature infants in the NICU (Barlow et al., 2008; Poore et al., 2008). The NTrainer technology was approved by the Food and Drug Administration in February 2008 and is scheduled for worldwide application in July 2009.

The NTrainer habilitation regimen includes a 10-day course of patterned orocutaneous therapy delivered during three scheduled feed sessions per day in the NICU. Our current NTrainer stimulus is delivered for a total of 9 minutes per gavage session (tube feeding) or 3 minutes preceding a bottle/breast-feed session. The training/stimulation provides the preterm infant with a trigeminofacial entrainment experience that is hypothesized to facilitate the development of a normalized suck. Use of an orocutaneous entrainment stimulus has the advantage of being safe and pleasurable for the neonate and easily administered by physician-provider-parent teams in the NICU, including developmental speech-language pathologists. Future work will explore the effects of multisensory inputs on oromotor and respiratory pattern formation in preterm infants during late gestation. The functional linkages between trigeminal inputs and swallow mechanisms are under study, including pharyngo-esophageal and gastric motility.

**Mapping sCPG development in utero via fetal MEG.** Our experience in developing real-time NTrainer suck waveform discrimination software algorithms was put to the test in a new bioimaging application to record NNS in utero via fetal MEG (Popescu, Popescu, Wang, Barlow, & Gustafson, 2008). Several studies in term and preterm infants have investigated the rhythmic pattern of NNS indicating correlations between the quantitative measures derived from sucking pressure variation or electromyographic recordings and a range of factors that include age, perinatal stress, and sequelae. In the human fetus, NNS has been observed from 13 weeks of gestation exclusively on the basis of real-time Doppler ultrasonography. In our study, we provide evidence that ororhythmic pattern production resembling NNS in the fetus can be reliably recorded and quantified via noninvasive biomagnetic measurements that have been recently introduced as an investigational tool for the assessment of fetal neurophysiological development. Source separation techniques, such as independent component analysis, applied to high-resolution multichannel recordings allow for the segregation of an explicit waveform that reflects the biomagnetic equivalent of the ororhythmic sucking pressure variation or electromyographic signal recorded in infants. This has enabled
morphological study of NNS patterning over different temporal scales, from global quantitative measures to within-burst fine structure characterization, in correlation with fetal cardiac rhythm.

Effects of upper lip revision surgery in children with orofacial clefts on facial animation, force dynamics, skin sense, and reflex modulation. Clefting of the upper lip is a significant health problem in the United States occurring on the order of 1 in 1,000 live births. These patients exhibit severe and obvious disfigurement of the upper lip and nose. Treatment is provided by a specialized, multidisciplinary team of clinicians and begins typically before 6 months of age and continues for about two decades. It is widely recognized, however, that this correction is only partially successful. Patients often require additional lip surgeries (two on average but as many as three or four) and nose surgeries before an aesthetically acceptable result is obtained, and there is questionable agreement among clinicians regarding when exactly this endpoint is reached.

Traditionally, decisions for each additional revision surgery are based solely on the morphology of the face at rest (evaluation of static form). Because physiological considerations are not incorporated into the decision-making process, there has been no impetus to investigate the motor and sensory function of the repaired lip in these patients. Moreover, it is unclear whether the revision surgery substantially improves facial appearance during function (dynamic form), another typical situation for which aesthetics is most important to an individual.

An NIH-funded clinical trial has been under way since 2001 (principal investigator: C. A. Trotman; sub-principal investigator: S. M. Barlow) to objectively measure and quantify facial motor and sensory function in the cleft patient to establish more rational, functionally relevant criteria for revision surgeries. Specific aims include systematic investigation of nasolabial form and motor and sensory function in the cleft lip patient with a set of measures developed at the CNL, including electrophysiological measures of perioral reflex modulation (Andreattia, Barlow, & Finan, 1994; Andreattia, Barlow, Finan, & Biswas, 1996; Barlow, 1991; Barlow & Bradford, 1996; Barlow, Finan, Bradford, & Andreattia, 1993; Estep & Barlow, 2007), orofacial fine force dynamics (Barlow & Abbs, 1986; Barlow & Burton, 1990; Trotman, Barlow, & Faraway, 2007), and biomechanical measures of perioral stiffness (Chu, Barlow, & Lee, in press; Seibel & Barlow, 2007). The working hypothesis is that the dynamic form and function of the nasolabial region remain severely altered in repaired cleft patients, and, although contemporary revision surgery may improve lip morphology at rest (static form), motor and sensory function as well as dynamic form may not be improved but may become even worse. If function and dynamic form are found to be worse, then subtle improvements in the aesthetics of the lip at rest after revision surgery may not outweigh the tissue-induced decrement in motor and sensory function. If this is the case, rational surgical decisions should incorporate functional considerations.

As a means of approaching this working hypothesis, unilateral and bilateral cleft lip and palate patients from the University of North Carolina Craniomaxillofacial Center, along with an age- and gender-matched noncleft control sample of regular patients at the School of Dentistry, are being followed for a period of 1 year (viz., 0, 6, and 12 months). A proportion of the unilateral and bilateral patients will undergo lip revision surgery shortly after “Time 0.”

Results from the force dynamics studies indicated that the upper and lower lips of the participants with a cleft lip demonstrated less time on target, whereas the lower lips had shorter rise times but higher peak forces, a higher rate of force recruitment, and increased maxima of the first derivative of force relative to the noncleft participants (Trotman et al., 2007). In the case of all participants, there was a learning effect for certain force variables between the two visits and with increasing age. Among participants with a cleft lip, force regulation of the circumoral region within the operating range presumed important for facial
and speech animation is compromised because of impairments in force recruitment, gradation, fractionation, and stability. In the presence of a change in upper lip tissue mechanics due to scarring or neuromotor impairment, such as a cleft, the lower lip typically exhibits compensatory motor actions. Analyses of tissue biomechanics (stiffness) and reflex modulation are under way.

**Translational Neurotherapeutics**

With the development of a therapeutic entrainment application well under way in human infants, we have invested considerable time and resources to explore how the brain encodes ororhythmic motor activity and its response to the NTrainer’s unique patterned orocutaneous stimulus properties in young adults. The translational applications are moving along a path towards new interventions for probilation in infants and children with developmental disorders and motor rehabilitation in adult patients who have sustained brain strokes or manifest certain forms of progressive neuromotor disease. Some of these exciting applications are described briefly in the paragraphs to follow.

Advancing neuroimaging applications to map shared neural networks and develop connectivity models in humans during speech and suck. During the past 2 years, specialized stimulation and blood oxygen level-dependent (BOLD) response sampling protocols for use with adults have been developed at the University of Kansas and implemented at the Hoglund Brain Imaging Center at the university’s medical school (Barlow, Lund, Estep, & Kolta, 2009; Estep et al., 2007, 2008; Estep, Barlow, Auer, Kieweg, & Savage, 2009). Our most recent functional magnetic resonance imaging (fMRI) work has focused on mapping cortical and subcortical (particularly brainstem and cerebellum) networks in healthy adults during production of ororhythmic speech and suck tasks as a function of rate (Estep et al., 2009). Details of this major study are summarized in Estep and Barlow’s article in this issue. Significant task- and rate-specific activations were identified by multiple regression analysis and then compared via conjunction analysis to identify common or task-specific areas (or both). The fMRI BOLD activation data overlaid on the anatomical image revealed that task- and rate-specific encoding neural correlates are extensive, with many shared neural loci apparent for speech and suck ororhythmic motor activities between putative brainstem relays, cortical loci (orofacial S1-M1, SMA, and BA 44), thalamic ventroposteromedial nucleus, globus pallidus internus, and cerebellum (deep nuclear and hemispheric activations; Estep et al., 2009).

**Innovative forms of sensory input to drive/modulate motor processes: Phased array somatosensory stimulation.** The human brain is highly adaptive and plastic, especially after cerebral insults such as stroke or lesions (Nudo, 2007). The brain has a remarkable capacity to adapt its structure and function in response to learning and enriched sensory environments (Ward, 2005). Sensory and behavioral experiences can dynamically alter the motor cortex in rats (Donoghue, Suner, & Sanes, 1990) and squirrel monkeys (Nudo, Milliken, Jenkins, & Merzenich, 1996) and produce lasting changes in the sensory cortices of monkeys (Byl, Merzenich, & Jenkins, 1996; Clark, Allard, Jenkins, & Merzenich, 1988). Thus, modulation of afferent inputs may play a major role in the plasticity of the sensorimotor cortex (Ridding, Brouwer, Miles, Pitcher, & Thompson, 2000).

Sensory experiences, including tactile and proprioceptive stimuli, improve motor performance and enlarge motor maps and behavioral repertoires. Conversely, lack of sensory experience due to amputation, nerve lesion, or neglect (deprivation) negatively alters motor map representations (Donoghue, Sanes, Hatsopoulos, & Gaal, 1998; Nudo, Plautz, & Frost, 2001; Sanes, Suner, & Donoghue, 1990). Cerebrovascular strokes or injuries to the brain that induce both motor and somatosensory deficits are more severe and incapacitating and delay motor function recovery (Reding & Potes, 1988). Individuals with only motor deficits respond better to rehabilitation interventions (Celnik, Hummel, Harris-Love, Wolk, & Cohen, 2007). Somatosensory stimulation preceding a training session has been observed to improve the
effects of training on use-dependent cortical plasticity in patients with a single ischemic stroke (Sawaki, Wu, Kaelin-Lang, & Cohen, 2006). Patterned, natural cutaneous somatosensory stimulation imitating a “salient” motion (i.e., related to speech, suck, gesture, and so forth) may substitute for motor training (Meegan, Aslin, & Jacobs, 2000; Planetta & Servos, 2008). In the absence of formal motor training, sensory training may operate to enhance motor plasticity and accelerate recovery during rehabilitation.

In most studies to date, electrical stimulation has been used to assess sensory training effects on motor rehabilitation. For example, subthreshold electrical stimulation of the whole hand for 30 minutes with a mesh glove followed by a simple finger tapping motor task has been shown to result in an increase in activation of primary and secondary motor areas and somatosensory areas in both hemispheres (Golaszewski et al., 2004). Electrical stimulation improves the motor and sensory functions in chronic stroke patients (Peurala, Pitkanen, Sivenius, & Tarkka, 2002). Stimulation of the paretic hands or feet of chronic stroke patients with a similar electrode over a period of 3 weeks has been shown to improve limb function, decrease the time required to perform functional motor tasks, and enhance sensation in the paretic limbs. Electrical stimulation can also lower muscle tone and improve spasticity in paretic limbs (Dimitrijevic & Soroker, 1994).

Limitations of electrical or electromechanical devices in the imaging environment. Electrical stimulation has the disadvantage of producing electrical interference and imaging artifacts in a magnetic resonance (MR) environment. Piezoelectric transducers (Gizewski et al., 2005) have good frequency response but possess limited displacement amplitudes. Furthermore, the presence of electric current necessary to drive the piezoelectric crystal results in interference inside an MR or MEG scanning environment, representing a significant technical challenge in recording from orofacial systems that are proximal to the MR head coil. Disk vibrators (Kawahira et al., 2004; Shirahashi, Matsumoto, Shimodzono, Etoh, & Kawahira, 2007) operate at a single frequency (83 Hz) and are impractical for use in MR and MEG. Air-puff stimuli delivered to the face and fingers via an MR-compatible manifold have enabled localization of the somatotopic representations of the face, lips, and fingers in the primary motor cortex, ventral motor cortex, and primary and secondary somatosensory areas (Huang & Sereno, 2007). However, patient positioning and calibration issues relative to the complex arrangement of electronic manifolds used for air-puff stimulation (Huang & Sereno, 2007) and pneumatic stimulation (Dresel et al., 2008) are difficult and time consuming and may preclude the study of sensory processing and motor reorganization among normal children, children with developmental disabilities, and adults with neurological conditions.

Translation to the adult orofacial model. To extend the previously discussed NTrainer approach for facilitating oromotor function to an adult model, we have designed a new method of activating somatosensory mechanoreceptors for use in either the MEG or fMRI scanner environment with a servo-controlled pneumatic tactile membrane that we call the “TAC-Cell” (Barlow & Venkatesan, 2009; Venkatesan, Popescu, & Barlow, 2009). We are currently using a 151-channel MEG to characterize the somatosensory cortical activation response after application of patterned cutaneous stimuli to the face with the TAC-Cell technology.

The TAC-Cell proof of concept is being tested in young normal adults to a tactile stimulus train consisting of a repeated six-pulse train with a 50-ms pulse duration and an intertrain interval of 5 seconds to explore mechanisms of short-term adaptation and cortical localization. Pulse rate within a train is varied across conditions at 2, 4, and 8 Hz. Dipole localization of the response within the primary somatosensory cortex is obtained by coregistering the current source with the anatomical MRI images obtained for each participant. Spatial activation peaks of sensor signals in response to tactile stimulation are obtained through current density analysis. Bilateral activation of S1 has been observed for stimulation of midline-lip vermilion. Current source localization via proprietary software packages has revealed strong activation responses in the sensorimotor region. Spatial activation peaks
appear to undergo significant modulation and adaptation as a function of the frequency of the stimulus and pulse index number. At this writing, we conclude that TAC-Cell stimulation of the glabrous surfaces of the face is highly effective in activating the sensorimotor cortex and other subcortical areas, including the ventroposterior thalamus.

TAC-Cell output is scalable in amplitude and frequency and programmable to provide a wide variety of patterned inputs to soft tissue surfaces. This will permit our team to explore basic and applied questions concerning how and where somesthetic inputs are processed in the brain, as well as characteristics of short- and long-term adaptation, localization, and experience-dependent network modification, and to document the effects on fine motor control in both normal and neurologically impaired children and adults. To achieve these goals, CNL bioengineers and scientists are developing an MR/MEG-compatible phase array TAC-Cell stimulation system that can produce the sensation of apparent motion on the skin’s surface. This approach will be tested in healthy children and adults and developed as a potentially new intervention for motor rehabilitation in children with movement disorders of the hand and face, sensory processing/attention issues (e.g., autism), or both.

Compelling evidence in the motor rehabilitation literature suggests that delivery of salient patterns of sensory stimulation alone is a potent neuromodulator of motor architecture and functional recovery. TAC-Cell stimulation and its variants are hypothesized to modulate plasticity and reorganization of the sensorimotor cortex and accelerate recovery of motor function during rehabilitation in stroke patients in lieu of motor training. This concept has far-reaching implications for a variety of movement disorders associated with developmental articulation disorders, dysarthria (speech motor), swallowing disorders and treatment (dysphagia), sensory integration disorders (autism), musculoskeletal or craniofacial genetic disorders (cleft lip, Down’s syndrome), response to injury (stroke, traumatic brain injury), and certain forms of progressive neuromotor disease (i.e., brain reorganization after deep brain stimulation in Parkinson’s disease).

**Summary**

The CNL is now 25 years young and counting. I have thoroughly enjoyed the voyage and thrill of discovery associated with dozens of experiments concerned with the sensorimotor development and control of orofacial and laryngeal systems subserving speech, vocalization, suck, and aeroingestive behaviors in health and disease across the human life span. A key ingredient in the multidimensional study lines described in this review is the assembly and nurturing of a strong multidisciplinary research team involving students and research faculty from communication sciences, biology, neuroscience, bioengineering, computer science, neurology, radiology and medical physics, neonatology, nursing, pediatrics, and physical therapy. Where possible, project lines are directed toward patient-oriented research and innovative interventions aimed at driving mechanisms of brain plasticity to improve communication/oromotor function, neurodevelopmental outcomes, or both.

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The Connectivity of Orofacial Systems

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Abstract

Acknowledging the dynamical properties of neural networks allows insight into the functional segregation and integration of cerebral areas. From a theoretical viewpoint, the complexity of neuronal interactions within a distributed system may reflect its capacity to rapidly process multimodal information and modulate context-sensitive neural activity to encode perception and adaptive behavior. This article highlights recent studies aimed at understanding the functionally flexible connectivity of the orofacial substrate.

Introduction

Although mapping cognitive processes to discrete brain areas has been the vanguard of functional neuroimaging studies for more than 20 years, contemporary theory emphasizes the interactions among distributed brain regions as the key mechanism by which overt behavior and cognitive functions are produced (Bressler, 1995; Friston & Price, 2001). Model-based or data-driven analyses of functional data have allowed investigators to characterize dynamic patterns of neural activity evoked during distinct stages of cognitive or motor tasks at the macroscopic level (D’Esposito, Postle, & Rypma, 2000; Kincses et al., 2008; Li, Guo, Nie, Li, & Liu, 2009; Price, Laird, Fox, & Ingham, 2009) or during rest (Mantini, Perrucci, Del Gratta, Romani, & Corbetta, 2007).

The notion of neural connectivity among remote brain areas changing as a function of cognitive and sensorimotor tasks has encouraged novel analytical methods to survey how disparate brain regions, or “nodes,” communicate with each other (Bullmore & Sporns, 2009; Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Seminowicz & Davis, 2007). One such analytical method, known as functional connectivity, is a description of temporal synchronization of brain regions indicative of the strength of relationships between regions (Friston, Frith, Liddle, & Frackowiak, 1993). After an anatomically constrained model of a known neural network has been characterized, the influence one region has on another (i.e., effective connectivity) can be modeled as a function of task or cognitive demand (Friston, Frith, & Frackowiak, 1993).

Connectivity analyses have become a popular approach in electrophysiology and neuroimaging studies for providing a measure of temporally correlated or task-dependent
linkages (or both) between distributed brain regions. Although the time scales and nature of measurements differ between functional imaging and electrophysiological studies (i.e., seconds vs. milliseconds and hemodynamic vs. spike trains, respectively), the coherence among active neural networks during cognition and sensorimotor processing is in agreement across these two measurement methods (Rissman, Gazzaley, & D'Esposito, 2004; Sun, Miller, & D'Esposito, 2004). To reveal underlying connectivity in electrophysiology studies, it is often necessary to remove confounding effects of stimulus-locked transients that present extraneous correlations that are not causally mediated by direct neural interactions. The confounding effect of stimulus-evoked transients is less problematic in neuroimaging studies because propagation of the brain's signals is mediated by neuronal connections that are usually reciprocal and interconnecting. One clear advantage of connectivity analyses over other techniques for studying temporal correlations among brain regions is the reduction of time-series data into parameter estimates that contain the information most critical in assessing interregional connectivity. More data are needed on human mapping to improve connectivity studies given that objective constraints are often based on neuroanatomical information from primate studies and cannot invariably translate to the human brain (Bullmore et al., 2000).

The Context-Sensitive Neuronal Response

Neuroanatomical and electrophysiological studies support the notion that cellular-level evoked responses are context dependent, meaning the brain is capable of making conditional inferences about sensory input (Abbott, Varela, Karmel, & Nelson, 1997; Kay & Phillips, 1996). At the systems level, a region may show similar activity patterns across tasks yet be part of different networks, producing different behavioral outcomes (Bressler & Kelso, 2001). “Cognitive context” refers to a particular pattern of functional connectivity, or pattern of interregional connections, and has been studied in paradigms of learning and awareness demonstrating that the pattern of neural interactions shapes the exact nature of behavior. For a given sensory cue, attention modulation changes the cognitive context of neurons to different perceptual attributes (McIntosh, Rajah, & Lobaugh, 1999, 2003; Treue & Maunsell, 1996). The frequency response can vary between and within brain networks while the participant is at rest, suggesting that multiple independent spontaneous oscillations coexist (Friston & Price, 2001; McIntosh, 2000; Wu et al., 2008).

Components of distributed networks have been hypothesized to serve multiple roles, including integration of convergent inputs and modulation of the neural activity of other network components. The notion of one area coordinating the activity of other distributed network components (i.e., variable effective connectivity) as a function of cognitive goal is supported by Bitan and colleagues (2005). They demonstrated task-dependent lexical processing of phonological versus orthographic information within a distributed language network. Afferent signals were routed from the inferior frontal gyrus to specific network loci of either the lateral temporal cortex or intraparietal sulcus. The inferior frontal gyrus was suggested to be a nodal point for coordinating activation of other network components in a task-specific manner (Bitan et al., 2005).

Shared and Unique Correlates of Oromotor Behaviors

Speech behaviors including syllable, word, sentence, and unvoiced articulatory gestures have been hypothesized by some to share correlates of nonspeech behaviors such as sucking, chewing, tongue/lip movements, and whistling. Each of these motor outputs requires a range of sensorimotor coordination (Brown et al., 2009; Lund & Kolta, 2006; Riecker et al., 2000). Shared neural correlates such as cortex, basal ganglia, thalamus, and cerebellum have been hypothesized to be differentially recruited for speech (Bohland & Guenther, 2006; Riecker et al., 2005) and nonspeech (Dresel et al., 2005) behaviors. Specific network activations are influenced by articulatory sequencing, as well as rate and effort, and they manifest a rate-
dependent hemodynamic response (Riecker et al., 2000; Riecker, Kassubek, Groschel, Grodd,
& Ackermann, 2006). Despite shared neuromusculature, opposing views suggest that
functionally specific ensembles of muscles and joints are centrally represented, and it has been
hypothesized that central encoding of speech is entirely unique from nonspeech behaviors
(Weismer, 2006; Ziegler, 2003). This view is supported by clinical reports indicating that
training on nonspeech oral behaviors is not effective in enhancing speech production, although
the issue of comparable operating ranges for force and movement is rarely considered in
comparisons of nonspeech training tasks with the dynamics of speech motor control.

Model-free connectivity analyses of adaptive functional changes within networks related
to learning a motor sequence have revealed independent networks including a temporally
modulated fronto-parieto-cerebellar network and a separate network consisting of the posterior
parietal and premotor cortices. Strengthening of the functional interactions among motor,
premotor, parietal, and cerebellar regions is specific to behavioral improvement secondary to
learning of a motor sequencing task (Kincses et al., 2008). Temporal modulation of network
activity related to task-associated repetitive behaviors may be part of a neurophysiological
“pruning” mechanism fundamental to learning a new skill (Kelly & Garavan, 2005).
Characterizing the interactions of functional networks relevant to motor sequence learning
tasks could provide insight into how distributed brain areas are functionally integrated to
encode oromotor sequencing.

Functional connections between neocortical and visceromotor systems strongly
implicate a distributed neural substrate for the self-monitoring and adaptive modulation of
patterned behaviors that constitute human vocalization (Schulz, Varga, Jeffires, Ludlow, &
Braun, 2005). In neonatal mammals, suck and other orocrhythmic motor behaviors appear to
be controlled by a network of interneurons localized to the central gray of the pons and
medulla (Tanaka, Kogo, Chandler, & Matsuya, 1999). This network, known as the suck central
pattern generator (Barlow & Estep, 2006; Barlow, Lund, Estep, Kolta, 2009), has been
identified in preliminary functional neuroimaging studies of human orofacial pathways (Estep
et al., 2008). Further investigation is anticipated to provide insight into common and unique
distributed neural resources correlated to speech activity that have the capacity to also drive
some of the functional synergies involved in producing suck behavior, such as the thalamus,
basal ganglia, insula, cerebellum, and pontomedullary region.

Innovations in Brain Connectivity Analysis

Interactions among different brain regions are maintained by functional connections
between regions reflecting the brain’s symmetric interhemispheric connections, functional
networks, and resting state networks (Toro, Fox, & Paus, 2008). A novel method to reveal
functional connectivity is to assess low-frequency (<0.1 Hz) hemodynamic fluctuations from
single-slice functional magnetic resonance imaging (fMRI) time-series acquisitions (Biswal,
Yetkin, Haughton, & Hyde, 1995). Analyzing interregional interactions in fMRI data collected
while the participant is not explicitly engaged in a cognitive task, referred to as resting state,
is quickly becoming a common strategy to test connection hypotheses with data obtained from a
single study. The low-frequency fluctuations in local field potential are presumed to be driven
by thalamocortical afferents or corticothalamic connections (Leopold, Murayama, & Logothetis,
2003).

Resting state networks may comprise a finite set of baseline or “default” interactions
from which task networks are then dynamically assembled during different behavioral states
and recruited by specific types of cognitive or sensorimotor processes (Damoiseaux et al., 2006;
De Luca, Beckmann, De Stefano, Matthews, & Smith, 2006; Taylor, Seminowicz, & Davis,
2008). The resting state networks of temporally correlated brain regions include an internal
processing network (Greicius et al., 2003), dorsal attention network (Corbetta & Shulman,
Connectivity in Human Development

Connectivity not only allows specialized regions to communicate with each other but also influences activity-dependent connections that are established and retracted between local cortical architecture and distal brain regions. In this way, connectivity plays a role in the development of functional and structural organization of neuronal tracts as seen in developing thalamocortical white matter tracts (O’Leary & Nakagawa, 2002). Increased myelination and the strengthening of connections through coactivation have been suggested as possible mechanisms driving the maturation of long-range connections that occur throughout adolescence (Fair et al., 2007). Establishing a developmental trajectory of functional connectivity is anticipated to provide an index of brain maturation that may be particularly useful for investigating neurodevelopmental disorders.

Age-related changes in the brain’s structural and functional organization have been demonstrated in at least five functionally distinct networks from late childhood to early adulthood (Kelly et al., 2009; Thatcher, Walker, & Giudice, 1987). The dissimilarity in oscillation frequency among different networks may reflect variable spontaneous neuronal firing rates or patterns that coexist to sustain the connections of a resting network (Wu et al., 2008). The frequency-specific and anatomic-dependent properties of functional networks may provide insight into the sensitivity and specificity of the resting-state fMRI signal and the development of functional connectivity. For example, impaired local cortical architecture and reduced long-range connectivity between cerebral regions have been hypothesized to affect sentence comprehension and executive function in individuals with developmental disorders (Belmonte et al., 2004; Just, Cherkassky, Keller, Kana, & Minshew, 2007; A. Mizuno, Villalobos, Davies, Dahl, & Muller, 2006; Turner, Frost, Linsenbardt, McIlroy, & Muller, 2006).

Future Directions

Recent attention has been directed to cross-system interactions and adaptive control among central pattern generating networks that support suck, swallow, and respiration in late-gestation (preterm) and term infants (Barlow, 2009a, 2009b; McFarland & Tremblay, 2006). An infant’s oral feeding skills benefit from early nonnutritive sucking experiences (Abbasi, Sivieri, Samuel-Collins, & Gerdes, 2008; Bingham, Thomas, Ashikaga, & Abbasi, 2008; Lau, 2006). Entrainment, or phase locking of a centrally generated motor pattern to an external stimulus, is one method to achieve neural synchrony among sensorimotor pathways, and it has been achieved during respiration (Sammon & Darnall, 1994) and task-specific nonnutritive and nutritive suck oromotor behaviors in preterm infants (Barlow, Finan, Lee, & Chu, 2008; Poore, Zimmerman, Barlow, Wang, & Gu, 2008). The effects of central neural pathology combined with systemic prematurity are presumed to adversely affect the circuits that regulate aerodigestion. Early feeding problems may contribute to significant delays in the emergence of other oromotor behaviors, including babbling and speech-language production (Adams-Chapman, 2006; Ballantyne, Frisk, & Green, 2006), and serve as a biomarker for neural integrity and neurodevelopmental outcomes (K. Mizuno & Ueda, 2005).

Barlow and colleagues are working to characterize the central mechanisms coordinating the lips, tongue, jaw, pharynx, and esophagus to orchestrate aerodigestion in the nursing infant. New methods are currently being used to assess central connectivity of orofacial systems, including multimodal stimulus interventions for the probabilitation of infant and pediatric populations with feeding disorders.
Summary

Local specificity and connectivity are two features of any given neurodevelopmental process. Complementary investigations of the temporal correlations between brain areas may provide insight into brain organization that is distinct from conventional functional imaging. There are growing numbers of studies supporting the validity of low-frequency correlations for mapping functionally specialized networks distributed cortically and subcortically, such as the motor network (Biswal et al., 1995; Xiong et al., 2009) and networks for language and memory (Hampson, Peterson, Skudlarski, Gatenby, & Gore, 2002; Lowe, Dzemidzic, Lurito, Mathews, & Phillips, 2000). Functional correlations among brain regions identified via paradigm and motor training-based functional neuroimaging approaches (McIntosh et al., 1994; Strother et al., 1995) can also be co-registered with resting-state scans (Lowe et al., 1998; Xiong et al., 2009). In addition, resting-state scan methods can be adapted to assess network connectivity in infants or other participants who cannot follow paradigm instructions.

Clinical data do not provide a full account of neuroanatomical correlates of articulatory/phonetic sequencing and processing. Functional imaging offers an alternative approach to address the sensorimotor aspects of speech production. In considering the role of functional connectivity in shaping anatomical connectivity through plastic changes (Sporns, Tononi, & Edelman, 2000), communication neuroscientists are encouraged to study common and task-specific central activations correlated to oromotor behaviors within a salient operating range for task dynamics (e.g., force, rate of force change, displacement, velocity, pressure and volume velocity, start and end-point specification) to gain a better understanding of the potential relationship to sensorimotor dysfunction in clinical disorders. This approach is likely to further our understanding of motor speech disorders and ultimately enable greater precision in diagnosis and guidance for more effective oromotor intervention methods involving specific oromotor tasks. Special attention is needed when examining these approaches, with careful consideration and assessment of the physiological operating range of the behavior in question, whether it is regarded as speech or nonspeech in nature.

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References


Orofacial Biomechanics and Speech Motor Control

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Abstract

The mechanical properties (e.g., mass, stiffness, viscoelasticity) of bone, cartilage, muscle, tendon, ligament, fat, and skin among articulatory subsystems involved in speech and gesture collectively influence all aspects of movement and must be accounted for in the selection and sequencing of motor program elements. Damage or disease processes affecting peripheral or central nervous system function, or both, can affect muscle coordination and alter muscle stiffness. Therefore, the biomechanics of orofacial and vocal tract structures should be taken into account when considering the movement patterns and network signaling in the neuromotor control system in health and disease. The purpose of this report is to summarize our evolving approach to and application of orofacial biomechanics in the context of movement disorders associated with dysarthria and craniofacial anomalies. We describe a new application for mapping stiffness in the lips for clinical application in pediatric and adult populations.

Introduction

The Greek philosopher Aristotle (384 BC–322 BC) is reported to have written the first book on biomechanics, *De Motu Animalium* (On the Movement of Animals), with particular attention to the various modes of locomotion exhibited by animals that fly, swim, walk, and move by other means. Aristotle provided the first reference to prime movers known in contemporary literature as “agonists” and reference structures (structures to support the body, or “postural control”), the utility of joints, and the concepts of sense perception and memory (Aristotle, 1978, 2007), quite a remarkable set of insights for the time. Nearly 2,000 years later, Giovanni Alfonso Borelli (1608–1679), a Renaissance Italian physiologist, physicist, and mathematician who is considered by some to be the father of modern biomechanics, published two papers, *De Motu Animalium I* and *De Motu Animalium II* (Borelli, 1989; Encyclopædia Britannica Online, 2009). He related animals to machines or mechanical systems and used mathematics to describe the relations between force and movement, center of gravity, and dynamics. Today, it is generally recognized that the biomechanics inherent to limb and orofacial systems play a significant role in our movements and are reflected in the stream of motor coding that defines adaptive and predictive control by the nervous system.
The speech motor apparatus includes the chest wall, larynx, pharynx, and orofacial musculoskeletal subsystems, which are driven by a dynamically assembled network of excitable tissues distributed among cerebral, deep brain, cerebellar, and brainstem structures (Barlow, Finan, Andreatta, & Boliek, 2008). Localized damage to even small portions of this modulated neuronal network can alter the activation, selection, and sequencing of constituent subsystems or influence postural regulation, with deleterious consequences for speech movements and intelligibility (Guenther, Ghosh, & Tourville, 2006). Unlike the limbs, key articulatory muscle systems for speech routinely undergo three-dimensional conformational change (tongue, lips) with sufficient spatiotemporal precision and pace to produce several vowels and consonants. The degree, nature, and rate of oral tissue conformation are important variables shaping the articulators for speech. For example, fractionated activation of subpopulations of motor units within the orbicularis oris muscles can produce lip closure, lip rounding, anterior lip protrusion, and even aversion of the lips (Müller, Milenkovic, & MacLeod, 1985). Because a lesion to either the central or peripheral nervous system can result in differential effects on speech motor subsystems, knowledge about the performance of these component articulatory systems is important in localizing the lesion site, monitoring change and plasticity over time in response to activity-dependent or stimulus-dependent interventions, and better understanding the resultant effects on speech motor control.

Limb System Organization

More than four decades of electrophysiological study in a variety of animal and human models support the notion of the central representation of muscles and their dynamics (force end point, rate of force change, position end point, and velocity). Functional neuroimaging studies have elaborated this view to reveal the extensive bilateral networks involving multiple regions of the brain, which modulate according to task dynamics and reorganize in the case of disease. Some investigators presume that the underlying dynamics (e.g., torques, forcing functions) related to biomechanics are ultimately reflected in expression of movement, and they are estimated with inverse modeling techniques. Similar approaches and principles may apply for speech, albeit second-order mechanics are notably different between the mass-dominant limbs and the relatively low-mass articulatory subsystems.

Muscles that move limbs in space or adjust the position of the spinal column and pelvic skeletal anatomy are typically organized around joints. These muscles (extrafusal fibers) rely on muscle spindles (intrafusal elements), Golgi tendon organs, joint receptors, and a variety of rapidly conducting mechanoreceptors to convey proprioceptive, cutaneous, and deep sense information to the motor control system, which minimally consists of the cerebellum, deep brain nuclei, brainstem, and sensorimotor cortices. The interplay of two major forms of motor control—regulation of postural control of axial muscle systems and phasic control signals for purposive movements (manipulation, locomotion, and speech-vocalization)—results in a repertoire of movement that is the single most important mode of biological expression. The phasic control process involves the selection, sequencing, and modulation of pyramidal tract neurons in Layer 5 of the sensorimotor cortex. Descending axons from these neurons course through the internal capsule and decussate (medullary level, ~95%; spinal cord, ~5%) to ultimately form monosynaptic connections with lower motor neurons and premotor inputs to integrative local circuits.

Most target muscles of the limb and trunk have tendinous attachments to bone and use proprioceptors such as muscle spindle receptors and Golgi tendon organs to regulate stiffness around the joints for postural and voluntary movements. During controlled movement in the extremities, muscle pairs (agonist and antagonist) work in coordination to produce intended patterns of movement. Recent studies on the primate motor cortex have demonstrated common end-point encoding regardless of limb starting position, suggesting the presence of motor attractors or common movement repertoires (i.e., hand-mouth, midline grasp and
manipulation, lateral reach, and so forth; Graziano & Aflalo, 2007). These findings indicate that the central representation of movement pattern generating networks may reside within the primary motor cortex.

**Perioral System Organization**

The trigeminal system (CN V) is a mixed constellation of fiber pathways and nuclei consisting of afferents, which segregate into three divisions (ophthalmic, maxillary, and mandibular), and an efferent branch in the mandibular division that innervates the muscles of mastication (Gardner, Martin, & Jessell, 2000). Orofacial cutaneous mechanoreceptors are composed of rapidly adapting type I receptors and slowly adapting type I and II receptors (Barlow, 1987; Johansson, Trulsson, Olsson, & Westberg, 1988). These perioral mechanoreceptors are innervated by rapidly conducting Aβ myelinated afferents coursing within the maxillary and mandibular divisions of the trigeminal system (Dodd & Kelly, 1991). Proprioceptive and kinesthetic information encoded by these mechanoreceptors is represented somatotopically in the trigeminal chief sensory nucleus located in the dorsolateral pontine tegmentum (Olsson, Sasamoto, & Lund, 1986).

The dorsal, medial, and ventral subdivisions of the chief (principal) sensory nucleus receive afferents from the mandibular, maxillary, and supraorbital divisions of the trigeminal nerve, respectively (Dodd & Kelly, 1991). For trigeminal representations involving the lower two thirds of the face, afferent axons from the chief sensory nucleus decussate and form the ventral trigeminothalamic tract (trigeminal lemniscus) and project to the contralateral ventroposteromedial nucleus of the thalamus, with subsequent relay to the primary face somatosensory cortex (S1). Within the contralateral ventroposteromedial nucleus, the upper lip is represented ventrally and the lower lip is represented dorsally (Kaas, 1990). The primary area receiving somatosensory information from the rapidly and slowly adapting mechanoreceptors of the contralateral face is located in the lateral postcentral gyrus of S1.

Alpha motoneurons associated with cell bodies located in the trigeminal motor nucleus send fibers to the tensor veli palatine \( m_\), tensor tympani \( m_\), and masticatory muscles (McComas, 1998). An additional cranial nerve system playing a major role in facial animation is the facial nerve (CN VII). Motor fibers that innervate the muscles of facial expression arise from the somatotopically organized facial nucleus located in the ventral portion of the pontine brainstem. CN VII fibers pass medially and arch dorsally, forming a loop or genu around the abducens nucleus before reaching the lateral surface of the pons and emerging as the facial nerve (Haines, 2004). Unilateral lesions of the facial nerve produce ipsilateral negative signs, including fasciculation and hemifacial paralysis.

The upper and lower lips are capable of opposing alternating movements at velocities approaching 25 cm per second during speech production. Although some muscles of the perioral mask have their origins in maxillary and mandibular bone, many slips of muscle that make up the interdigitating orbicularis oris muscle system insert directly into the semitendinous node of the oral angle or deeper layers of the glabrous and nonglabrous skin of the lips, cheek, and chin. Perioral muscles also lack the classic proprioceptor arrangement and presence of muscle spindles and golgi tendon organs (Folkins & Larson, 1978). Thus, the organizational plan for the “floating” facial mask is quite unique from its limb counterparts. Some of the distinct anatomical and biomechanical features of perioral muscles are as follows (Barlow, 1987, 1998; Blair & Müller, 1987; Blair & Smith, 1986; Kennedy & Abbs, 1979; Müller et al., 1985):

- Muscle fibers often lack fascia and tendon connections to bones of the lower skull.
- Muscle fibers do not have well-defined insertion points.
- Muscle fibers vary greatly in plane and orientation.
• Most muscle fibers originate from the maxilla and mandible with insertion into the integument surrounding the mouth.
• The perioral muscles, integument, and skin have a unique anatomical relationship to $A_\beta$ mechanoreceptors that encode motion sense, pseudo-form proprioception, and cutaneous sensibility for encoding the consequences of speech and nonspeech movements.
• Unlike the limbs, the perioral tissues can be modeled as a predominantly viscoelastic system, with the mass term exerting negligible inertial effects on typical speech movement acceleration functions.

Orofacial Biomechanics

There are at least three sources of force acting on muscle-tissue systems of the vocal tract: the external forces arising from the environment (gravity, fixtures, perturbations, and aerodynamics); the forces generated as subpopulations of motor units, driven by complex patterns of tonic and phasic inputs; and the forces resulting from the biomechanical properties of a given articulatory subsystem. The latter may be due to inertial loads (mass dependent), viscous loads (velocity dependent), or elastic loads (stiffness dependent). Thus, coordinated motor output depends on a nervous system that has benefited from experience during changes in body plan to account for task dynamics, biomechanics, and environmental loads. The interactions among these force fields, task dynamics, and biomechanics have been investigated extensively for limb movements and, to a lesser extent, for mandibular movements.

Stiffness, defined as the measurement of resistance to displacement, is affected by the central neural inputs, reflexes, muscle properties, and the geometry of muscle attachments (Shiller, Laboissière, & Ostry, 2002). The biomechanical properties of bone, muscle, cartilage, skin, and adipose tissues of the articulators, including their mass, viscosity, and stiffness, significantly influence movement (Sanguineti, Laboissière, & Ostry, 1998). Shiller and colleagues (2002) examined the effects of jaw stiffness on kinematic variation during speech and observed that the pattern of jaw kinematic variation during simple CVC utterances was related to the spatial pattern of jaw stiffness. For higher jaw elevation, stiffness was greater and kinematic variability was reduced. The stiffness field played an important role in shaping kinematic variability for jaw movements. Relatively little is known about the influence of biomechanical factors on orofacial movements during speech, ingestive, and mimic behaviors in spite of their ecological importance for survival.

Clinical Application of Orofacial Biomechanics

In our view, there are several applications of orofacial biomechanics that hold considerable promise for clinical assessments of and interventions involving neuromotor speech disorders. For example, an accurate measurement of force tetany combined with study of force recruitment functions can provide useful information on the integrity of descending inputs and access to the lower motor neuron pool. One quantitative method for measuring stiffness involves imposing a specific displacement ($\Delta X$) on a muscle-tissue system and measuring the resultant force ($\Delta F$). The ratio of the resultant force to displacement yields a stiffness quotient ($\Delta F/\Delta X$). On the basis of this principle, muscle rigidity, regarded as a clinical correlate of stiffness, has been used to evaluate neurological status and document the effects of disease progression, pharmacological treatment, and neurosurgical interventions (Prochazka et al., 1997; Sepehri et al., 2007).

In two recent studies, quantitative measures of perioral stiffness were sampled during a nonparticipatory (no contraction) task involving a wall-mounted, computer-controlled linear motor servo programmed to impose a series of tensile displacements over a span of approximately 24 mm at the oral angle in both female and male adults (Chu, Barlow, & Lee, in
press; Seibel & Barlow, 2007). Both male and female participants manifested a quadratic growth in interangle lip stiffness as a function of interangle span. Polynomial nonlinear regression revealed that male adults had a significantly increased stiffness profile relative to female adults over the same range of imposed lip displacements. These two studies also demonstrated that real-time data acquisition and analysis of perioral stiffness during a “do not contract” nonparticipatory condition can be completed within 30 seconds in cooperative participants. The methods used, however, require head stabilization in a cephalostat for several minutes during presentation of lip displacements. Although this sampling procedure was effective with cooperative healthy participants, this instrumental approach precludes study of facial biomechanics in patient populations where dyskinesia is an issue secondary to progressive neuromotor disease or traumatic brain injury or in pediatric populations with orofacial movement disorders associated with facial clefts.

As a means of solving these problems, a perioral-referenced interangle device known as OroSTIFF was developed in our bioengineering laboratory to examine the feasibility of real-time perioral stiffness measurements in unrestrained participants. The OroSTIFF device incorporates a pneumatic glass air cylinder actuator instrumented for pressure and an integrated subminiature displacement sensor to encode lip aperture. Real-time calculations of the perioral stiffness function (Chu, Barlow, Kieweg, & Lee, 2008) demonstrated a significant quadratic relation between imposed interangle stretch and resultant force. These results indicate that interindividual variability in stiffness growth functions increases as the interangle span increases (Chu et al., 2008). This may be because of individual differences in the anatomical structure of the perioral system that contribute to differences in the individual stiffness slope. The increase in stiffness is due to elasticity of muscle and connective tissue within the perioral system, up-regulated by a heightened level of tonic electromyographic activity that is relatively constant and independent of interangle span. This stiffness growth function also differed significantly between male and female participants.

**Future Directions**

This study demonstrates the OroSTIFF “proof of concept” for cost-effective, noninvasive stimulus generation and automatic derivation of perioral stiffness in healthy unrestrained adults. We applied this same method in a case study to illustrate the dose-dependent effects of Levodopa on perioral stiffness in an individual with advanced Parkinson’s disease who exhibited marked dyskinesia and rigidity. Currently, OroSTIFF is being evaluated in a randomized clinical trial involving children undergoing lip revision surgery associated with clef lip. The next logical step is to test this application in patients with facial movement disorders associated with progressive neuromotor disease (i.e., Parkinson’s disease, amyotrophic lateral sclerosis, and cerebellar disease), neuroinflammatory conditions (multiple sclerosis), craniofacial anomalies (cleft lip), or acquired insults to the nervous system (stroke, traumatic brain injury, bomb blasts, and missile injuries).

Mathematical models of orofacial biomechanics are needed to better understand how the brain may optimize these features of the perioral force plant in the planning and execution of muscle performance and movements during speech. Translating bench applications for the measurement of select biomechanical variables (e.g., force, force velocity, stiffness, tetany) to high-speed, real-time bedside or clinical assessments will enhance our knowledge of the dynamics of movement and may lead to new intervention strategies for individuals with movement disorders of the lower face. Moreover, it is our position that a patient-referenced biomechanical “tool set” will provide the clinician with a new set of diagnostic measures that can be used to monitor the effects of interventions (e.g., functional stimulation, surgery, pharmacological interventions) in the treatment of movement disorders affecting speech motor control.
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References


Suck Predicts Neuromotor Integrity and Developmental Outcomes

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Abstract

Neonatal motor behavior predicts both current neurological status and future neurodevelopmental outcomes. For speech pathologists, the earliest observable patterned oromotor behavior is suck. Suck production requires effective coordination of an infant’s oral sensorimotor system and is subject to a variety of neuromodulatory inputs. Demonstration and practice of coordinated suck serves as a biomarker for oral feeding skills neural integrity and is being assessed for its relation to neurodevelopmental outcomes (speech, cognition, and learning) by research teams in the United States, Europe, Japan, and Brazil. Suck may also serve as an intervention point to prevent feeding disorders and mitigate speech-language delays and disorders.

Neuromotor Development in Utero

Neuromotor development begins in the womb. Infants kick, stretch, push, suck fingers and toes, swallow amniotic fluid, and exercise the chest wall in utero before any of these behaviors are functionally required at birth. These early motor behaviors are essential to drive developmental processes. Spontaneous movements activate populations of mechanoreceptors and sensory end organs, forming a volley of sensory flow that is encoded and transmitted along lemniscal pathways. This rich information characterizes the state of the developing fetus and its immediate surroundings and plays a crucial role in the refinement of neural connections via accurate motoneuron path finding and precise molecular expression (Hanson & Landmesser, 2004).

One of the first oromotor behaviors to occur in the womb is suck, which begins from the gestational age of 15 to 18 weeks (Miller, Sonies, & Macedonia, 2003). Across all fetal and neonatal movements, mouth opening and hand-to-mouth movements are among the most frequent (Kurjak et al., 2004). The behaviors the infant expresses in utero establish and strengthen neural pathways that will later become important for learning and perfecting motor behaviors such as eating, speaking, and gesturing.
Sucking Ability and Neuromotor Integrity

Suck becomes stable and well patterned by the postmenstrual age of 34 weeks (Hack, Estabrook, & Robertson, 1985). It can be either nonnutritive (NNS) or nutritive. NNS consists of a series of cyclic compression cycles separated by pauses. A collection of consecutive compression cycles is known as a burst. Each burst consists of 4–12 suck cycles produced at approximately 2 Hz (Estep, Barlow, Auer, et al., 2008; Finan & Barlow, 1996; Urish, 2008). Nutritive sucking is produced at a slower rate (~1 Hz) than NNS, with fewer or no interburst pauses (Wolff, 1968), and it requires additional coordination of swallowing and respiration (Barlow, 2009b). Nutritive suck is characterized by alternation of suction (creation of negative intraoral pressure) and expression (compression and stripping action of the tongue against the nipple), both of which will draw milk into the oral cavity (Amaizu, Shulman, Schanler, & Lau, 2008; Lau, 2006, 2007).

Pattern formation for ororhythmic output is driven by the suck central pattern generator, with the minimal circuitry consisting of bilateral networks of interneurons residing between the trigeminal motor nucleus and the facial nucleus in the central gray of the brainstem (Tanaka, Kogo, Chandler, & Matsuyama, 1999). Coordinated suck depends on descending cortical input, intact brainstem pathways, reciprocal connections with the cerebellum, and appropriate sensory input from oral mechanoreceptors (Barlow & Estep, 2006; Barlow, Lund, Estep, & Kolta, 2009).

Suck requires an intact nervous system and appropriate environmental experiences if it is to be coordinated and functional in the infant. Suck reflects an infant’s current neuromotor status and is also an important functional behavior for the infant. A functional suck is presumed to be an essential precursor to successful oral feeding.

An ever-increasing population of infants who exhibit poor sucking skills are preterm infants. There are many reasons why preterm infants have poor suck, including the unexpected and often maladaptive extrauterine environment of the neonatal intensive care unit. A preterm neonate’s gestational age alone is a direct predictor of nutritive sucking skill and feeding maturation (Amaizu et al., 2008). Preterm infants’ ability to suck has a substantial impact on their health, state control, and developmental outcomes, and it can have a significant impact on the family and community as well. Preterm infants (born before the gestational age of 37 weeks) currently make up nearly 13% of live births in the United States, with the average medical cost for each very-low-birthweight infant well above $200,000 (Schmitt, Sneed, & Phibbs, 2006). The longer the infant is in the hospital, the greater the cost, and one of the primary reasons for preterm infants’ protracted hospital stays is their inability to suck and feed orally.

One group of preterm infants with especially poor suck is those with neurological impairments. Infants who have neurological damage and perinatal distress have significantly slower mean NNS rates and greater intraindividual NNS rate variability (Dreier & Wolff, 1972). Also, infants with cerebroventricular hemorrhage and ventricular dilation produce less consistent NNS than their healthy counterparts (Burns et al., 1987). Damage to cortical, subcortical, and brainstem pathways can obliterate suck or cause substantial disorganization or atypical expression of suck.

Preterm infants who have respiratory disease and require extensive oxygen therapy in the neonatal intensive care unit (NICU) also demonstrate poor suck. Research has shown that preterm infants who have been intubated and required oxygen therapy exceeding 1 week perform poorly on the Neonatal Oral Motor Assessment Scale (Bier, Ferguson, Cho, Oh, & Vohr, 1993), a subjective measure of sucking ability. They also have poor spatiotemporal coordination of suck pressure trajectories when evaluated with the Non-nutritive Suck Spatiotemporal Index (Poore, Barlow, Wang, & Lee, 2008), exhibit reductions in NNS burst
pattern performance (Estep, Barlow, Vantipalli, Lee, & Finan, 2008), and manifest reduced NNS amplitude (Stumm et al., 2008) relative to peers without respiratory disease. These infants regularly experience abnormal tactile stimulation of the perioral, intraoral, and nasopharyngeal tissues during extended periods of intubation and cannulation (Comrie & Helm, 1997).

Trussing the orofacial apparatus with feeding tubes and oxygen tubes limits movement and sucking. This exposes the already-fragile premature infant to unexpected and maladaptive sensory inputs that must be endured during oxygen therapies. This form of sensory deprivation and motor restriction can disrupt development of the motor cortex and cerebellum, which are essential for normal sensorimotor control (Pascual, Fernandez, Ruiz, & Kuljis, 1993; Pascual & Figueroa, 1996; Pascual, Hervias, Toha, Valero, & Figueroa, 1998). Such atypical input to the trigeminal sensory system is unexpected and detrimental during this critical period of oromotor development in infancy.

There is ample evidence indicating that high-risk infants, such as those with extensive oxygen treatment histories or neurological damage, have poor oromotor coordination for sucking. However, recent research shows that even low-risk premature infants (gestational age of more than 30 weeks, normal birthweight) often have poor suck (Silberstein et al., 2009). In particular, low-risk premature infants who have abnormal neurobehavioral functioning, including poor reactivity to stimulation, poor motor responses, and poor state control, tend to have more feeding difficulties, slower suck rates, and lower feeding robustness (Silberstein et al., 2009). This group of low-risk infants with abnormal neurobehavioral functioning, poor sucking skills, and difficulties in transitioning to oral feeding represents more than one third of low-risk premature infants (Silberstein et al., 2009). Clearly, suck has a tight link to neurodevelopmental status and is an important sensorimotor skill in infant development (Barlow, 2009b; Lau, 2006; Mizuno & Ueda, 2005).

**Sucking Ability and Neurodevelopmental Outcomes**

Suckling skills not only are highly predictive of infants’ current neurological status but may also predict their future neurodevelopmental outcomes. Early suck skills can independently predict problems that do not manifest in an infant’s behavior until much later in development and can therefore serve as a valuable diagnostic indicator. For example, infants who manifest poor suck coordination are likely to exhibit cognitive delays and complex motor delays (Mizuno & Ueda, 2005). An organized suck pattern at the postconceptional age of 34 weeks predicts a preterm infant’s degree of bodily coordination and fine motor skills at 6 months of age (Medoff-Cooper & Gennaro, 1996). In a retrospective study of a cohort of infants evaluated with the Neonatal Oral Motor Assessment Scale, all infants who demonstrated developmental delay (cognitive, motor, or speech-language) at 24 months had a history of neurological damage, poor sucking ability, or both (Palmer & Heyman, 1999).

One important perceptual-motor behavior that has been linked to early sucking ability and that has an especially protracted expression is speech-language production. Neonates (gestational age of 35-42 weeks) with low sucking pressure and an inability to coordinate expression and suction within a couple weeks of birth tend to have speech-language delays at 18 months (Mizuno & Ueda, 2005). Early problems with sucking and feeding in extremely low-weight preterm infants have also been found to lead to significant delays in the emergence of speech-language production (Adams-Chapman, 2006; Ballantyne, Frisk, & Green, 2006). Across all ages, speech pathologists regularly observe that clients who have poor feeding skills tend to have poor speech-language skills as well (Morris & Klein, 1987).

Suck, feeding, and speech-language production are encoded and modified by overlapping networks of cortical, subcortical, and brainstem regions. These oromotor behaviors are produced with many of the same muscles and are modulated by mechanoreceptors from the same epidermal surfaces and deep connective tissues. This evidence has led many to
predict that the neural networks that control suck, swallowing, and feeding also control aspects of speech production (Barlow, 2009a; Barlow et al., 2009; Estep, Barlow, Auer, et al., 2008; Lund & Kolta, 2006; McFarland & Tremblay, 2006). If the degree of overlap and functional connectivity between these systems is significant, then success with early sucking and feeding skills may provide an essential foundation for successful speech-language production.

**Evaluation of Suck**

One substantial advantage of evaluating suck is that it is a precocial motor behavior. Assessments of suck represent one of the most accessible and earliest possible analyses of an infant’s neuromotor status. Currently, the earliest stage at which speech and language skills can be reliably predicted is at the onset of canonical babbling (Oller, Eilers, Neal, & Schwartz, 1999; Stoel-Gammon, 1992), which is approximately 6 months (Eilers et al., 1993; Stark, 1980). Like suck, babble is characterized by rhythmic movements of the mandible (Davis & MacNeilage, 1995) and requires precise coordination of oral and vocalization muscle subsystems. The ororhythmic patterning for suck may represent the most salient biomarker of speech-language ontogeny and may be indicative of a critical period for early intervention.

Physiological evaluations of suck provide essential information on neural integrity and sensorimotor skill development that is not provided by other assessment techniques during late gestation and term-equivalent age. For example, Mizuno and Ueda (2005) found that assessment of feeding performance had better sensitivity and specificity in predicting neurodevelopmental outcomes than ultrasound assessment. Measures of suck motor patterning also have been found to have higher predictive sensitivity and specificity than measures of neonatal morbidity (Medoff-Cooper & Gennaro, 1996). This indicates that precise analyses of suckling provide a diagnostic value superior to that of other neonatal assessment techniques.

There is a need for sensitive, quantitative, and efficient analyses of suck among preterm infants in the NICU (de Costa, van den Engel-Hoek, & Bos, 2008; Lau & Kusnierek, 2001; White-Traut, Berbaum, Lessen, McFarlin, & Cardenas, 2005). Unfortunately, the analytical tools for suck development in most NICUs are based on subjective judgment. The clinician may place a gloved finger in the infant’s mouth to estimate rhythmicity, strength, cycle frequency, and burst duration (Comrie & Helm, 1997; Lau & Kusnierek, 2001). There are obvious limitations to this approach, including reliability within and between examiners and an inability to access the fine structure of pressure dynamics, variability of suck patterning, and developmental progression.

A new biomedical device called the NTrainer has been approved by the Food and Drug Administration for real-time quantitative analysis of the NNS motor pattern among preterm and term infants in the NICU (Barlow, Finan, Chu, & Lee, 2008). Digitally sampled suck compression waveform records are analyzed in real time for several parameters, including suck cycle periods, amplitude, duration, NNS burst structure, and discrete Fourier transforms. The NNS Spatiotemporal Index can also be calculated from suck compression waveforms. This index, which quantifies spatial and temporal variability across suck pressure trajectories, has been used successfully to classify suck motor pattern formation among preterm infants with varying degrees of respiratory disease (Poore, Barlow, et al., 2008). This is also a very useful technique to document the effects of probalbilitation techniques on ororhythmic pattern formation (Poore, Zimmerman, Barlow, Wang, & Gu, 2008).

A comprehensive assessment of infants’ neurodevelopmental status and outcomes must have a consistent and objective set of procedures for administering and scoring, should be capable of being used alongside intervention programs to evaluate treatment efficacy, and must be longitudinal so that developmental progression can be frequently and accurately monitored.
Neurodevelopmental evaluation techniques should also be cost effective and time efficient. Many standardized examinations and neuroimaging procedures do not satisfy this need. However, evaluation of suck, in particular with the NTrainer technology, satisfies each of these essential characteristics.

**Treatment Techniques**

Recognizing the predictors of neurodevelopmental outcomes allows for creation and modification of appropriate early treatment techniques. Although it is important to chart neurodevelopmental outcomes, there is an even more urgent need to take action to help prevent and treat problems before they occur. One method of providing preventative treatment of oromotor dysfunction is via oral or intraoral stimulation. Oral stimulation strategies (Fucile, Gisel, & Lau, 2002, 2005; Rocha, Moreira, Pimenta, Ramos, & Lucena, 2007) and the provision of a pacifier in early neonatal life (Volkmer & Fiori, 2008) have been shown to effectively develop both breast-feeding and bottle oral feeding skills in premature infants.

The NTrainer, in addition to being an assessment tool, is also used as an intervention tool to stimulate and entrain ororhythmic patterns via a synthetic pneumatic orocutaneous stimulus pulse train that closely mimics the expected pattern of suck during late gestation (Barlow et al., 2008). The NTrainer probahilitates infant suck by delivering patterned intraoral stimulation to entrain the infant’s ororhythmic activity and accelerate the development of NNS. The NTrainer essentially functions as a “pulsing pacifier” and can be adjusted to meet frequency and amplitude requirements for developmentally appropriate NNS patterns. Recent studies have shown that the NTrainer can be used to probahilitate the central patterning of suck among infants with limited or no functional oromotor output (Poore, Barlow, et al., 2008; Poore, Zimmerman, et al., 2008) and that this intervention in turn improves infants’ ability to feed successfully by mouth (Barlow et al., 2008). Future studies of early suck treatment techniques should examine their ability to reduce the occurrence of motor, cognitive, and speech-language delays. This approach is consistent with predictions that treatment of suck and feeding disorders has the potential to prevent or reduce the severity of certain forms of speech production disorders (McFarland & Tremblay, 2006).

Future research should also address the possibility of preventing speech-language delays and disorders by developing interventions suitable for the earliest stages of vocalization. The sequence of vocal development in the first year of life has been well researched, with good agreement on characteristics and stages demonstrated cross linguistically (Nathani, Ertmer, & Stark, 2006; Oller et al., 1999; Stoel-Gammon, 1992). However, far less research has been done on how to treat delays in prespeech vocalizations. Currently, the earliest prespeech stage that has been linked to speech-language delay is canonical babbling. Because the standard for provision of early speech-language therapy is that a child must demonstrate at least a 25%–50% delay to warrant services, most children are not provided speech-language intervention before 1 year of age. Clearly, the research indicates that oromotor development occurs from early stages of gestation and neonatal life, and efforts should be made to identify early biomarkers (predictors) and treatment techniques for oromotor behaviors such as suck and speech.

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The Complexity of Transitioning to Oral Feeds in Preterm Infants

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Abstract

Transitioning to oral feeds is one of the final tasks that preterm infants need to accomplish before discharge from the neonatal intensive care unit. There are many types of pacifiers and nipples used to accelerate and encourage the development of feeding skills; however, little is known about the impact of the mechanical properties of these nipples on feeding among preterm infants, who often must endure prolonged periods of sensory deprivation, maladaptive inputs, and motor restriction. Many feeding specialists alternate between different nipple types on a trial-and-error basis in an attempt to find the most appropriate nipple type for the infant. Given the complexity of feeding, a more comprehensive understanding of the multiple neural interactions among suck, swallow, airway protection, pharyngoesophageal motility, and digestive mechanisms is needed. Delay or disruption of these processes during a critical phase in late gestation may prevent infants from transitioning successfully to oral feeds and may lead to poor neurodevelopmental outcomes.

Proficient feeding is essential for an organism to thrive; however, it is often an arduous task for premature infants. The act of nutritive suck (NS) is a complex motor task produced at an average cycle frequency of 1 Hz (Barlow, 2009a; Finan & Barlow, 1996; Wolff, 1968), and it requires the coordination of suck, swallow, and breathing patterns (Bu’Lock, Wooldridge, & Baum, 1990). This intricate motor task also requires primary activity of five cranial nerves (V, VII, IX, X, and XII), spinal segments to drive the chest wall, and coordination of more than 30 pairs of muscles distributed across several physiological systems, including oropharyngeal, laryngeal, and respiration (Matsuo & Palmer, 2008; McFarland & Tremblay, 2006; Miller, 1982). Multiple central neural systems control NS, including brainstem central pattern generator (CPG) circuitry, which is primarily composed of adaptable networks of interneurons that activate lower motor neurons to generate task-specific motor patterns (Barlow, Lund, Estep, & Kolta, 2009), sensory feedback, and other subcortical and cortical control processes (McFarland & Tremblay, 2006). The ability to synchronize and coordinate the suck-swallow-
respiratory pattern is posited to reflect the state of motor system integrity and positive neurodevelopment.

During nipple feeding, mechanoreceptors in perioral and intraoral tissues encode salient features of the nipple, including shape, texture, stiffness, and temperature, along primary and lemniscal trigeminal projections. This rich stream of sensory flow serves to modulate the activity of the brainstem CPG (Lund & Kolta, 2006) and may provide the infant with important cues to reconfigure the CPG to meet changing task dynamics such as various nipple types and bolus volumes during feeding (Finan & Barlow, 1996; Lau, 2006, 2007). For example, initiation and modulation of the swallow can be triggered by activity in intraoral and pharyngeal sensory afferents via cranial nerves V and IX (Jean, 1990; Mistry & Hamdy, 2008). Sensory feedback plays a significant role in cross-system modulation of motor patterns among suck, swallow, and respiration, and as the organism matures it includes the mastication network (Barlow, 2009a).

Sensory CPG modulation is important for adaptation and probably helps the infant correct modal ororhythmic patterns to unexpected disturbances in the local environment, or it may be used to regulate nutritive flow rates during oral feed regardless of nipple orifice geometry (Barlow, 2009a; Barlow et al., 2009; Lau, 2006). The latter is particularly important in adjusting the temporal organization of the feed sequence to ensure a safe swallow. If a safe swallow is to occur, the epiglottis, aryepiglottic folds, and true vocal folds all need to adhere to a strict time sequence, thereby preventing penetration and aspiration of the bolus into the trachea and lungs.

The ability of preterm infants to adapt their swallow under different bolus loads may be reduced as a result of the effects of extended periods of sensory deprivation associated with oxygen dependency. During periods such as these, the infant is effectively restricted from auto-stimulation of the perioral sensorium (Estep, Barlow, Vantipalli, Finan, & Lee, 2008). A combination of maladaptive and reduced orosensory input may reduce the positive sensory experience essential for optimizing pattern formation and brain development during the presumed critical period of swallowing proficiency (Barlow, 2009b; McFarland & Tremblay, 2006).

The cerebral representation of orofacial movements and integrative processes is vital for adaptation of ororhythmic outputs in response to changing physiological and mechanical constraints (Barlow et al., 2009; McFarland & Tremblay, 2006). Many very-low-birthweight preterm infants experience cerebral lesions that may negatively affect all aspects of swallowing synchrony (McFarland & Tremblay, 2006). This not only makes feeding difficult but could potentially affect speech production later in development, in that distinct cortical areas may project to CPG circuits coordinating mouth and tongue movements essential for speech production (Dronkers, 1996; Hickok, 2001; Wise, Green, Buchel, & Scott, 1999). When considering the brain insults that can influence ororhythmic behaviors in the infant, the application of neurotherapeutic techniques that promote suck and feed skills is a favorable clinical option.

The experience afforded by nonnutritive suck (NNS) may enhance suckling skills and may accelerate the transition to successful oral feeds (Barlow, Finan, Chu, & Lee, 2008; Fucile, Gisel, & Lau, 2002; Lau, 2007; Pickler, Frankel, Walsh, & Thompson, 1996; Rocha, Moreira, Pimenta, Ramos, & Lucena, 2007). Suck maturation is accompanied by an increased ability to orally feed (Barlow, 2009b; Lau, 1992, 2006; Poore, Zimmerman, Barlow, Wang, & Gu, 2008). When infants experience prefeeding NNS stimuli, they demonstrate earlier readiness for the bottle, characterized by initiation of nutritive suck more quickly and maintenance of initial NS activity for a longer period (Pickler et al., 1996; Segal, Prakash, Gupta, Mohan, & Anand, 1990). Rocha and colleagues (2007) examined the efficacy of sensory stimulation in NNS among low-birthweight infants. Infants provided with an additional oral stimulation regimen began an
oral diet 8.2 days earlier, had their gavage use suspended 8.6 days earlier, and were discharged from the hospital 10.4 days earlier than the control group that received no additional oral stimulation. Furthermore, NNS experience is suggested to lead to enhanced weight gain and may result in a decreased length of stay in the neonatal intensive care unit (NICU) by several days (Field et al., 1982; Pinelli & Symington, 2000; Rocha et al., 2007; Segal et al., 1990).

The NTrainer, a new medical device approved by the Food and Drug Administration, was designed to entrain or rhythmic motor activity and provide salient cues to the infant on the temporal structure of "burst-pause" NNS patterning. This is achieved by providing patterned orocutaneous stimulation through a pressurized silicone pacifier designed to mimic the classic burst-pause sequence of NNS. This safe and ecologically valid form of oral stimulation is hypothesized to influence CPG drive and probably provides the infant with a salient sensory experience during a critical period of ororhithmic pattern formation and brain development. This unique intervention has been shown to accelerate NNS burst pattern formation (Foore et al., 2008), improve suck parameters, and help preterm infants transition faster to oral feeds (Barlow et al., 2008).

Feeding specialists, speech therapists, and occupational therapists work closely with the NICU care-provider team to help preterm infants transition successfully to oral feeds. Developmental care and infant positioning, along with state control and peripheral stimulation (e.g., NNS, ororhithmic entrainment via cutaneous, acoustic), can be used in combination with the many options for feeding nipple types (e.g., shape, size, flow rates) to facilitate the transition to safe oral feeds (Scheel, Schanler, & Lau, 2005). There are numerous feeding nipples to choose from, including Dr. Brown's®, Gerber®, Evenflow®, Nuk®, Haberman®, Soothie®, Similac®, Playtex®, and Enfamil®. Often alternating nipple types are used on a trial-and-error basis during different feeding sessions (Scheel et al., 2005).

After making the decision on what brand to use, feeding specialists and caregivers are faced with another set of decisions, including what size and flow type should be used. These choices become daunting given the paucity of objective data on how the use of these differing nipple types is encoded by the infant's nervous system and what changes the infant must make in force dynamics to compensate for the differing mechanical properties and flow rates of individual nipples for the proper compression and expression of milk (nutrient). For example, one study comparing three different bottle nipples to assess their impact on oral feeds did not identify a particular nipple that enhanced bottle feeding in very-low-birthweight infants. Infants were able to regulate the rate of milk transfer regardless of the feeding nipple aperture geometry (Scheel et al., 2005). Feeding therapists must also consider that the infant's behavioral state and performance during feeding are strongly influenced by environment and position and the caretaker's general approach to handling the infant. Together, these factors are essential for positive neurodevelopmental care and can significantly affect feed performance and development (Als, 1995; Barlow, 2009b).

Although providing early NNS experience is beneficial to the infant, not all pacifiers and nipple types are equal in performance. The physical characteristics of an object (e.g., finger, pacifier, nipple, or breast) placed in a newborn's mouth have marked effects on suck patterning and thus may affect oral feeding performances in unpredictable ways (Wolf & Glass, 1992). The type of nipple used affects the pattern of intraoral stimulation, and this can be especially problematic for infants who are poor feeders (Dubignon & Campbell, 1968). The size, shape, and compressibility of the pacifier/nipple have been shown to influence the frequency of NNS and NS (Dubignon & Campbell, 1968; Lipsitt & Kaye, 1965).

Recently, Zimmerman and Barlow (2008) observed that NICU graduates manifested a preference between two different models of popular NICU silicone pacifiers when tested at their 3-month follow-up. These infants tended to reject the Super Soothie® pacifier and displayed
little or no functional suck relative to ororhythmic activity on the regular Soothie® pacifier. Both pacifier models were tested for material stiffness, bulb volume, and geometry. When a position servo instrumented for force was used, compression tests on the nipple cylinder revealed that the Super Soothie® pacifier was 7 times stiffer than the Soothie® pacifier even though both pacifiers have identical external (outside) mold profile geometries and an oral displacement volume of 4 cc. Significant differences in ororhythmic patterning were observed as a function of pacifier type, including NNS cycles per minute, NNS amplitude, NNS cycles per burst, and NNS cycle periods (Zimmerman & Barlow, 2008). This cohort of infants clearly preferred the less stiff Soothie® pacifier and produced more complex NNS burst structures than the NNS output on the stiffer Super Soothie® pacifier.

Another intriguing finding of this study was that infants decreased suck rate in an attempt to accommodate the stiffer pacifier nipple. This demonstrates the adaptability of the suck CPG network to accommodate a change in a physical local environment. This form of orofacial modulation is probably encoded by trigeminal afferents projecting to brainstem pattern generating networks. Features of the local environment such as stiffness, texture, and shape are, in all likelihood, encoded as unique sensory signatures and serve to modulate the NNS pattern. Future studies on CPG adaptation mechanisms will benefit from this knowledge and may lead to the emergence of new intervention strategies to facilitate the transition to oral feeds in not only preterm infants but also other pediatric and adult populations with feeding disorders.

Prematurity in the United States continues to rise, with nearly 13% of all live births classified as preterm (gestational age less than 38 weeks). There is a need for systematic research on oral stimulation during late gestation and early infancy, with consideration given to the local environment and mechanical properties of various nipple types and their influences on feeding skills. In combination, the roles of sensory experience, neural maturation, critical periods, and neural integrity support the development of feeding and swallowing (McFarland & Tremblay, 2006) and may affect the emergence of babbling and speech development. Given the multisensory nature of feeding in infants, a more complete understanding is needed of cross-system neural interactions. It is hypothesized that delays in these processes may be a key factor limiting the transition to safe oral feeds, thus amplifying the risk for poor neurodevelopmental outcomes.

**Conclusion**

Suck and feed development in neonates and infants represents a relatively new topical area of study and practice within speech pathology and bears special relevance to brain-behavior mechanisms presumed to affect later emerging communication skills. Few graduate study programs in speech-language pathology offer formal course work in infant neurobiology or aeroingestive physiology. The NICU and feeding clinics are often overlooked as important clinical placements. This situation results in speech-language therapists who are anxious to work with this fragile population.

At the University of Kansas, we offer a comprehensive curriculum on human neurobiology, with related research and clinical experiences in the NICU and pediatric feeding clinics. To this end, our laboratory has created a study line to prepare individuals for the role of developmental speech physiologists that includes primary academic training in speech-language pathology, neuroscience, and neonatology. It is our view that a speech-language pathologist academically and clinically trained in developmental science and neurobiology can assume a key role in the NICU, assisting the late-gestation premature infant to develop state control and ororhythmic pattern generation to support safe swallow and promote neural integrity. Large-scale, randomized clinical trials are currently under way to measure the effects of early intervention involving multimodal patterned simulation on neurodevelopmental outcomes. We encourage speech-language pathologists working in the NICU and in the area of
infant development to survey the prolific literature on early feeding skills, early human
development, and new therapeutic interventions given that the emergence of translational
technologies holds significant promise in the probihabitation of the preterm infant.

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