Induced Unilateral Vocal Fold Paralysis and Recovery Rapidly Modulate Brain Areas Related to Phonatory Behavior: A Case Study

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Summary: Background. Peripheral and behavioral effects of voice disorders are well documented in the literature; yet, there is little information regarding the central neural biomarkers and mechanisms underlying these disorders. Understanding the details of brain function changes in disordered voice production is a critical factor for developing better treatment strategies that result in more robust patient outcomes.

Objective. To examine a model of induced unilateral vocal fold paralysis (iUVFP) to demonstrate and characterize the form of activity changes within central mappings of the larynx to the induced paralysis. The induced paralysis model allowed the participant to serve as his or her own control when comparing baseline results of normal voice with results during the paralysis and subsequent recovery.

Study Design. Prospective, case-study design.

Methods. Functional magnetic resonance imaging was used to examine central laryngeal representations during three time points: pre-iUVFP, during iUVFP, and postrecovery from iUVFP. iUVFP was induced using a lidocaine with epinephrine nerve block unilaterally. Percent changes in blood oxygenation level-dependent (BOLD) activity served as the dependent variable.

Results. Results indicated an overall reduced activity level in sensorimotor, subcortical, and cerebellar regions during paralysis. Recovery from paralysis led to augmented responses, particularly in sensory, association, and cerebellar zones.

Conclusions. The decrease in activity during iUVFP and the significantly increased activity during the recovery phase likely represent immediate neuroplastic events occurring within minutes of nerve blockade. Recovery-related changes in the BOLD response are hypothesized to be associated with a recalibration of the system after return of normal laryngeal function.

Key Words: Vocalization—Neuroplasticity—Voice disorder—Nerve block—Reorganization.

INTRODUCTION

Although much is known about the peripheral effects of voice disorders, little is understood of the relationship between behavioral features of voice disorders and the consequences of these features on central neural mappings. Because speech and language are uniquely human, the existing animal models are inherently limited in their capacity to represent human speech and skilled vocal performance. Methodological advancements in noninvasive neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and sparse sampling designs, are readily available and useful for overcoming significant artifactual obstacles in the study of production variables related to speech and voice.[1–4] As a result, data are now emerging on the characteristics of central representations of the larynx during human voice production and running speech. For example, studies by Haslinger et al,[1] Ozdemir et al,[4] Loucks et al,[3] and Huang et al[2] have all identified core brain regions activated during normal speech and voice tasks. These areas include, but are not limited to, the primary sensory and motor areas, anterior cingulate cortex, midline cerebellum, thalamus, and the periaqueductal gray region among others.

Few reports using neuroimaging techniques are available for those with disordered voice compared with normal vocal abilities. Of the work currently available on disordered voice populations, there is one report in persons with Parkinson disease[5] and another in spasmodic dysphonia[6] using positron emission tomography. fMRI[7] and diffusion tensor imaging[8] have also been used to study persons with spasmodic dysphonia, and a more recent case study was performed in a person with an acquired unilateral vocal fold paralysis (UVFP) using fMRI.[9]

The observed deleterious effects in voice quality and production consequent to disease and injury described in these studies demonstrate the value for understanding the central neural representation of the laryngeal system in both normal and disordered voices. Whether one studies the normal or disordered vocal behavior, understanding how the performance effects of behavior influence neural function and structure is critical to the development of optimal treatment strategies that will engender long-term functional restoration of voice when challenged with injury or disease.

UVFP is defined as the loss of mobility of one vocal fold because of injury and is most often attributed to peripheral nervous system lesions.[10] It may be caused by damage to the vagus nerve or one of its branches, the recurrent laryngeal nerve (RLN) or the superior laryngeal nerve (SLN).[11] Voice quality resulting from UVFP is often characterized by various degrees

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of hoarseness and significant increases in voice production effort. Treatment for UVFP typically entails surgical and/or behavioral management.[12]

The application of different forms of anesthesia has been used to simulate peripheral neural damage to assess the input- or output-related changes in cortical mappings in animal models[13] and in humans[14] (most often, the digits). These studies have found that during anesthesia, there is an areal increase in the representation of the intact body segment within the cortical representation zone of the anesthetized segment. Cortical mapping changes have been observed within a few minutes after anesthesia inducement.[15,16] On recovery, cortical representations have been observed to return to their original mapping, requiring a time course of a few minutes to hours for complete restoration.[13,14]

The input-dependent shifts in cortical activity during and after peripheral nerve blockade are suggested to be indicative of a latent anatomical network whose influence is revealed when dominant inputs are temporarily blocked. Projections from the thalamus to the cortex (thalamocortical) are known to have overlapping dendrite branching patterns that cross over representational boundaries of neighboring somatosensory zones in cortex. Observed changes to the size and form of central representations rely on the capacity to dynamically shift the balance of excitatory and inhibitory activity within and across representational boundaries, as afforded by the underlying anatomical and functional usage.[17]

Injecting the RLN with a nerve block solution of lidocaine HCL with epinephrine induces a temporary UVFP. In the 1970s and early 1980s, this procedure was routinely used clinically in patients with adductor spasmodic dysphonia (ADSD) to evaluate patient candidacy for nerve sectioning as a treatment for ADSD[18–21] and was first described by Dedo[18] in 1976. More recently, this procedure has been used to experimentally induce vocal fold paralysis to study muscle tension dysphonia and the results of SLN paralysis.[21,22] The present study is the first to use nerve block to temporarily induce UVFP to study the immediate cortical neuroplastic responses to a loss and subsequent recovery of vocal function. This experimental model allows the participant to act as his or her own control, because baseline measures can be obtained before the inducement of the UVFP. It is rarely, if ever, possible to obtain baseline measures in patients with UVFP. Consequently, the current model provides us with a unique opportunity to compare the immediate neuroplastic changes that occur after inducement of UVFP and during recovery from paralysis.

The purpose of this exploratory study was to use fMRI to characterize the central representation of the larynx at three time points: before an induced paralysis, during induced paralysis, and after recovery, within a single participant. This experimental model was used to demonstrate the form and time course of brain activity changes before paralysis, during paralysis, and on recovery. We hypothesized a decrease in activity in the sensorimotor regions during paralysis, with a return of activity levels similar to that observed during the preparalysis phase.

METHODS

Participant

A 57-year-old right-handed male participant with normal voice quality was recruited to test the model of using a temporary induced UVFP (iUVFP) to further our understanding of immediate short-term cortical changes. The study protocol was approved by the Institutional Review Board at the University of Kentucky. The participant signed a written consent form. The participant's normal voice quality was confirmed by perceptual evaluation, patient's self-report, and videostroboscopic examination, revealing normal appearance and function of the glottis. After an initial baseline fMRI scan, right vocal fold paralysis was induced using a 0.3-cc solution of lidocaine and epinephrine (1:100 000) delivered to the right RLN by a board-certified otolaryngologist. The presence of vocal fold paralysis was visually confirmed with a videostroboscopic examination (Figure 1) and through the perceptual presence of a severely hoarse vocal quality. After confirmation of paralysis, a second fMRI scan was then performed during the induced paralysis phase. One hour after recovery from the induced paralysis, as confirmed by a return to normal voice quality and a normal videostroboscopic examination, a third fMRI scan was performed using the same scanning protocol as in the previous two imaging sessions. Preinjection, postinjection, and postrecovery videostroboscopic examinations were performed using a Kay Elemetrics (Montclair, NJ) Rhino-Laryngeal Stroboscope (model RLS 9100 B) with a Kay Elemetrics 70° rigid endoscope (model SN 1541).

Functional magnetic resonance imaging paradigm and task performance

An event-related sparse sampling design was used to obtain fMRI data from the participant. The participant was instructed in a sentence-reading task that included the production of multiple trials of six phonetically balanced sentences from the *Consensus Auditory-Perceptual Evaluation of Voice* (*CAPE-V*; American Speech-Language-Hearing Association, Rockville, MD).[23,24] Two-sentence runs comprising a total of 60 trials of the sentence-production task were used during each functional scan. The instruction and stimuli were displayed onto a screen using commercially available software (*E-Prime*; Psychology Software Tools Inc., Pittsburgh, PA) and an MRI-compatible projection system (SilentVision SV-6011 LCD, Avotec Inc., Stuart, FL). The participant received instructions for each of the tasks projected onto a mirror attached to the head coil. A screen providing the instruction for the task to follow was presented for 3 seconds. The next screen provided the target stimulus, and the participant was instructed to produce the sentences displayed (eg, "Peter will keep at the peak") at a steady pace and at a comfortable loudness. The task time was jittered from 3.5 to 4.5 seconds to ensure capture of the hemodynamic response peak (Figure 2). The delayed latency of the hemodynamic response during the task allowed for an efficient use of an event-related design. The sentences within each run were pseudorandomized.