Functional Magnetic Resonance Imaging Study of Brain Activity Associated With Pitch Adaptation During Phonation in Healthy Women Without Voice Disorders

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Summary: Objectives. This functional magnetic resonance imaging (fMRI) study investigated the brain activity associated with pitch adaptation during phonation in healthy women without voice disorders.

Study Design. This is an interventional prospective study.

Methods. Sixteen healthy women (mean age: 24.3 years) participated in a blocked design fMRI experiment involving two phonation (comfortable phonation and high-pitched phonation) and exhalation (prolonged exhalation) tasks. *BrainVoyager QX* Version 2.4 software was used for group-level general linear model analysis (q[FDR] < 0.05).

Results. Analyses showed a significant main effect of phonation with pitch adaptation compared with rest period in the bilateral precentral gyrus, superior frontal gyrus, posterior cingulate gyrus, superior and middle temporal gyrus, insula and cerebellum, left middle and inferior frontal gyrus, right lingual gyrus, cingulate gyrus, and thalamus. Statistical results also identified a significant main effect of exhalation compared with rest period in the bilateral precentral gyrus, cerebellum, right lingual gyrus, thalamus, and left supramarginal gyrus. In addition, a significant main effect of phonation was found in the bilateral superior temporal gyrus and right insula, as well as in the left midbrain periaqueductal gray for high-pitched phonation only.

Conclusions. We demonstrated that a blocked design fMRI is sensitive enough to define a widespread network of activation associated with phonation involving pitch variation. The results of this study will be implemented in our future research on phonation and its disorders.

Key Words: phonation control–fMRI–sensory feedback–sensorimotor integration–vocal pitch.

INTRODUCTION

Human phonation is a laryngeal motor behavior that extends from reflexive laryngeal actions[1,2] to highly skilled laryngeal sensorimotor control to support speech or singing.[3] A component of normal phonation is the variation of voice pitch (habitual, high, and low). Integration of the sensory input and laryngeal motor output is required for pitch adaptation during vocalization.[4,5] Moreover, voice pitch variation necessitates coordination of the respiratory system, the articulatory system, and the subglottic pressure.[6–10] With regard to the laryngeal system, pitch adaptation depends on the interaction between intrinsic and extrinsic laryngeal muscles.[11–13] Using a wide pitch range contributes to the richness of human voice expression. People with vocal problems (like functional dysphonia) often have limited pitch ranges, such as a high and narrow vocal pitch interval due to laryngeal postural problems during phonation.[14–17] The prevalence of functional dysphonia is 41% in the working-age population (25–64 years), and female professional voice users are predominantly affected (43% women vs 36% men).[18] This has been the rationale to investigate the neural control of voice pitch variation in women.

Neuroimaging techniques have become important tools to describe neural networks associated with laryngeal control of phonation.[19–22] Recent functional magnetic resonance imaging (fMRI)[19–21,23,24] and positron emission tomography[22] studies have shown that in order to understand the neural control of phonation, laryngeal control must be investigated distinct from the neural correlates for voluntary exhalation control and oral articulation. These studies have identified the sensorimotor cortex region (corresponding to Brodmann area [BA] 1, 2, 3, or 4), premotor cortex region (BA 6 or 8), superior temporal gyrus (STG) (BA 22, 41, or 42), insula (BA 13), cingulate gyrus/cortex, supramarginal gyrus (BA 40), lingual gyrus (BA 18 or 19), thalamus, cerebellum, midbrain, and basal ganglia as key regions involved in non-disordered phonation[19–24] (Figure 1). More specifically, as defined by functional brain imaging, the sensorimotor cortex region functionally includes the primary motor cortex (BA 4) and primary somatosensory cortices (BA 1, 2, and 3), and is anatomically located on/in the pre/postcentral gyrus and central sulcus.[25] In addition, premotor cortex region functionally includes premotor cortex and supplementary motor area and is anatomically located on/in the precentral gyrus and superior/middle/inferior frontal gyrus (SFG/MFG/IFG).[25] The sensorimotor and premotor cortex regions, STG, and insula have been identified as key areas involved in the integration of sensory input and laryngeal motor output during vocalization.[26–29] Additionally, several studies have shown the neural basis of human pitch perception (sensory control)[30] in the STG and the neural basis of laryngeal motor control of vocal pitch modulation in the right IFG.[9] Studies such as these have advanced our understanding of the phonation control and vocal pitch modulation control. In addition, the fMRI study by Loucks et al (2007)[21] has

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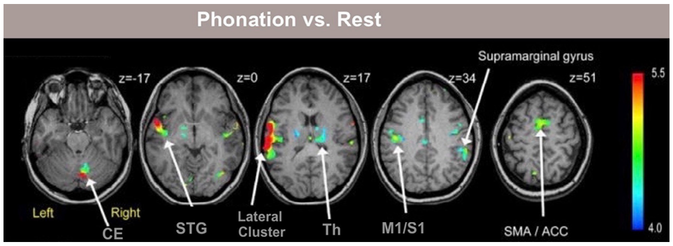

FIGURE 1. fMRI activations for phonation (modified from Loucks et al, 2007) onto the Talairach template brain; z coordinates are given below each slice ($P < 0.01$). Prominent cortical activations are found in the left lateral cortex extending from the IFG, through the postcentral gyrus to the STG (BA 1–4, 6, 22, 44; z = 17), the right cerebellum (z = −17), the right supramarginal gyrus (BA 40; z = 34), and the bilateral pre-/postcentral gyrus (BA 3, 4, and 6) in a region superior to the left ventrolateral cluster (z = 34) and the SMA (BA 6; z = 51), and extended into the ACC. Prominent subcortical activations are found in the ventral and medial nuclei of the right thalamus (z = 18). ACC, anterior cingulate cortex; BA, Brodmann area; fMRI, functional magnetic resonance imaging; IFG, inferior frontal gyrus; M1, primary motor cortex; S1, primary sensory cortex; SMA, supplementary motor area.

demonstrated that the neural control of exhalation for phonation is similar to the neural control of voluntary exhalation, only a difference in STG activation was seen due to the auditory feedback. However, the sensorimotor integration control during vocal pitch changes remains poorly characterized. This is in part due to the difficulties in identifying the sensory, motor, and sensorimotor aspects of phonation control in an experiment. In addition, phonation demands simultaneous control of respiratory, laryngeal, and articulatory systems in the production of various frequencies/pitches.[6–10] Thus, investigations aiming to isolate the neural mechanisms of laryngeal sensorimotor control of pitch modulation are particularly challenging. In the fMRI study by Peck et al (2009),[9] the production of neutral /uh/ sound at three vocal frequencies without labial and jaw movement was chosen. This experimental paradigm evaluated the laryngeal motor control of pitch adaptation in phonation with neutral vocal tract condition and minimal influence of jaw movements control and oral articulation. This approach was used in other fMRI studies with the production of /ə/ (schwa) sound, with focus on laryngeal gestures only[23,24] rather than sensory feedback. In other fMRI studies by Loucks et al (2007),[21] Haslinger et al (2005),[19] and Simonyan and Ludlow (2010),[31] the production of /i/ sound without labial and jaw movements was chosen. In this experimental paradigm, laryngeal sensorimotor control of phonation was evaluated that requires precise sensory feedback and articulatory adjustment of the vocal tract during phonation. The approach that used the production of /i/ sound to focus on the sensorimotor control of phonation with minimal influence of oral articulation and jaw movements control was used in our study.

The aim of this study was twofold: (1) to investigate the laryngeal neural control of phonation involving pitch (comfortable and high pitch) adaptation with minimal influence of voluntary respiratory control and oral articulation, and (2) to examine the usability of a blocked design fMRI method in defining the laryngeal neural control of phonation. In order to minimize the involvement of oral and pharyngeal muscles, we excluded tasks connected with laryngeal functions, such as coughing, swallowing, or speech. We implemented an experimental paradigm contrasting sustained phonation of unarticulated (ie, without spreading the lips) sound /i/ with prolonged exhalation using subtraction approach during the fMRI data analysis in order to focus on sensory feedback control of phonation. This approach is based on a study of Loucks et al (2007),[21] which showed that the neural control of exhalation for phonation is similar to the neural control of voluntary exhalation, only a difference in STG activation was seen due to the auditory feedback. These results were obtained by subtracting the neural control of voluntary exhalation from the neural control of phonation during the fMRI data analysis with a subtraction approach.[32,33] Additionally, the phonation tasks in this study explored the neural control associated with changes in pitch (comfortable and high). We hypothesized that a primary region related to phonatory activation would be the auditory cortex and that it can be observed as such by using fMRI. We focused on STG because it has been identified as an integration area of sensory input and motor output during phonation,[4,34] specifically during error detection and correction involved in pitch processing.[26,27,34–36] Furthermore, STG is involved in auditory-vocal integration and processing of predicted and actual vocal output.[37] The findings may provide a foundation for future investigations of pitch adaptation in phonation and its disorders.

MATERIALS AND METHODS

Participants

The study has been performed as an interventional prospective study. Sixteen healthy female, right-handed, native Flemish speakers (21–45 years old, mean age: 24.3 years) with no history of neurologic or psychiatric disease participated in the study. We reported the results of analyses performed on a cohort of 15 subjects. Subject 4 was excluded from analysis (data from functional scan were missing). Written informed consent was obtained from all participants. The same otorhinolaryngologist and speech therapist examined each subject clinically following a standard evaluation protocol. This protocol included the ENT (ear, nose, and throat) evaluation, videostroboscopic examination,[38] and the vocal quality evaluation by means of the dysphonia severity index (DSI).[39] Each subject had normal laryngeal structure and function on videostroboscopy. All participants had a DSI value higher than +1.6 (mean DSI: +3.5), which constitutes a normal voice quality.[39] In addition, samples of voice based on the production of a sustained vowel /i/ were recorded during voice evaluation, and the fundamental frequency (F0) and highest frequency (F-high) for each subject were assessed (mean F0 was 211.6 and mean F-high was 799.3 of the vowel /i/). Before scanning, participants filled in a prescan MRI safety questionnaire, the Edinburgh Handedness Inventory measurement scale, and a personal history questionnaire. These questionnaires have been used to select participants who satisfy the inclusion criteria, such as fMRI compatibility, participant characteristics, medical history, and lifestyle. After scanning, participants filled in a postscan MRI checklist, which asked for information on the effects of the MRI equipment and its environment (ie, magnetic field, acoustic noise) on scanned participants.