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Neuromagnetic detection of the laryngeal area: Sensory-evoked fields to air-puff stimulation

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ABSTRACT

The sensory projections from the oral cavity, pharynx, and larynx are crucial in assuring safe deglutition, coughing, breathing, and voice production/speaking. Although several studies using neuroimaging techniques have demonstrated cortical activation related to pharyngeal and laryngeal functions, little is known regarding sensory projections from the laryngeal area to the somatosensory cortex. The purpose of this study was to establish the cortical activity evoked by somatic air-puff stimulation at the laryngeal mucosa using magnetoencephalography. Twelve healthy volunteers were trained to inhibit swallowing in response to air stimuli delivered to the larynx. Minimum norm estimates was performed on the laryngeal somatosensory evoked fields (LSEFs) to best differentiate the target activations from non-task-related activations. Evoked magnetic fields were recorded with acceptable reproducibility in the left hemisphere, with a peak latency of approximately 100 ms in 10 subjects. Peak activation was estimated at the caudolateral region of the primary somatosensory area (S1). These results establish the ability to detect LSEFs with an acceptable reproducibility within a single subject and among subjects. These results also suggest the existence of laryngeal somatic afferent input to the caudolateral region of S1 in human. Our findings indicate that further investigation in this area is needed, and should focus on laryngeal lateralization, swallowing, and speech processing.

Introduction

The timely initiation of swallowing, coughing, breathing, and voice production/speaking depends on effective sensory input from the larynx. Unrecognized or insufficiently recognized sensations in the larynx, as seen in stroke patients, can lead to dysphagia, aspiration, and failure to evoke coughing, thereby resulting in a larger fundamental frequency response to pitch-shifted voice auditory feedback (Aviv et al., 1997, 1998; Canning et al., 2004; Larson et al., 2008). So far, a fiber optic endoscopic evaluation of swallowing with sensory testing allows for assessment of laryngopharyngeal (LP) sensation and provides information regarding severe LP sensory deficits and related matters (Aviv et al., 1996, 1998). A previous study using fMRI in patients with spasmodic dysphonia demonstrated significantly increased activation of the primary somatosensory cortex (S1) during symptomatic syllable production, characterized by involuntary laryngeal spasms (Simonyan and Ludlow, 2010). Therefore, elucidation of the sensory projections from the larynx to the somatosensory cortex is essential in developing an understanding of the pathophysiology of dysphagia and dysphonia caused by various central nervous disorders.

Magnetoencephalography (MEG) is a non-invasive measurement tool designed to detect magnetic fields generated by brain activity. The spatio-temporal resolution of MEG has led to continued growth in the understanding of oropharyngeal sensory processing (Gow et al., 2004; Nagamine et al., 1996; Tamura et al., 2008; Teismann et al., 2009b). While several studies using neuroimaging techniques in humans have reported the somatotopy of the pharynx (Furlong et al., 2004; Teismann et al., 2009b), the projections of the superior laryngeal nerve (SLN) and the vagus nerve from the larynx to S1 remain unknown. In MEG studies, the primary problem with estimation of cortical activity produced by laryngeal stimulation is the difficulty associated with discriminating activations generated by laryngeal stimulation from the mixed activations caused by artifacts produced by bodily movement surrounding the mouth and neck. The purpose of this study was to detect laryngeal somatic responses in both time and space using MEG. Therefore, the primary focus was on measuring laryngeal somatic responses with a higher signal-to-noise (S/N) ratio. A secondary focus was on addressing several issues necessary for the identification of somatotopic locations after laryngeal stimulation.

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Materials and methods

Subjects

Twelve healthy volunteers participated in this study (5 females, age range 23–42 years, mean age 32.6 years). None of the participants had a history of ontological or neurological disorders. The purpose of the experiment was fully explained to the subjects and all subjects provided written informed consent for participation in the study. The study design was approved by the Ethics Committee of Kyushu University.

Stimulation

Fig. 1 shows a schematic view of the experimental procedures with respect to stimulation and MEG recording. A flexible laryngoscope was inserted into the nasal passage and the distal tip of the scope was advanced to confirm the location of the tip of a tube, approximately 3–5 mm from the center of the arytenoid region (Aviv et al., 1998) (Fig. 1, top left). Since it was difficult to stimulate each arytenoid region separately by using air-puff stimulation through the tube, we attempted to set the tube near the center of the arytenoid region, which is the lowest part of the laryngeal vestibule. To allow for adaptation to the laryngoscope, a 1-min rest period was provided for all subjects. The air pressure level was adjusted according to the psychophysical technique of the ascending–descending method of limits (Aviv et al., 1996). A stimulus with a 200 ms duration and a 0.5 Hz frequency was used. Stimuli were delivered to each tube (3 in total) in random sequence to avoid habituation. Initially, a supra-threshold stimulus level, easily detected by the subjects, was presented to the site in the larynx. To confirm stimulus detection, the subjects were required to raise their arms within 2 s of stimulus presentation. For each detection trial, a descending sequence of pressure stimuli was presented twice and an ascending sequence of pressure stimuli was presented once. The laryngeal sensory recognition threshold (SRT) was defined as the lowest detection pressure at which each subject made 3 consecutive correct answers. For the confirmation of somatotopic mapping from different body locations, the right buccal mucosa and the right index finger were also stimulated using tactile stimulation. Additionally, MEG measurements were performed using stimulus levels lower than the SRT in 6 subjects.

Video monitoring and training

Prior to the experiment, the subjects were trained to inhibit swallowing, chewing, and movements of the neck, nose, and mouth. Before the first measurement, each subject was requested to inhibit bodily movement surrounding the mouth and neck as much as possible. Video monitoring (PowerLab, ADInstruments, Colorado Springs, CO, USA) was conducted to confirm each subject's behaviors during the measurements. A key point of the training was to instill in the subject an understanding of the influence of bodily movement using the video images and distorted MEG signals, and to dissuade the subject from performing these bodily movements through repeated warnings. For each subject, the measurements were performed on 2 separate days. On the first day, after collecting a couple of runs as training, the results were shown to the subject. On the second day, the analyzed video images and signals from the first day were shown to the subjects. In addition, if the subject still showed bodily movements, the results for the quick analysis of the video and signals were carefully fed back to each subject verbally during the 5-min rest period. Furthermore, after recruiting well-trained subjects, typical examples of video data from previous subjects were presented to the subjects prior to starting the first measurement.

MEG recording

Laryngeal somatosensory evoked magnetic fields (LSEFs) were measured using a whole-head 306-channel biomagnetometer system (Elekta-Neuromag, Helsinki Finland) in a quiet, magnetically shielded room. Prior to the recording, 4 head-position indicator (HPI) coils were attached to the scalp and a 3D digitizer (FASTRAK, Polhemus, Colchester, VT USA) was used to estimate the positions of the HPIs, and to obtain the shape of the head. Magnetic responses were digitally sampled at 1000 Hz. The time delay from the trigger to the onset of air-puff emission from the tube was 36 ms, which was fixed by an

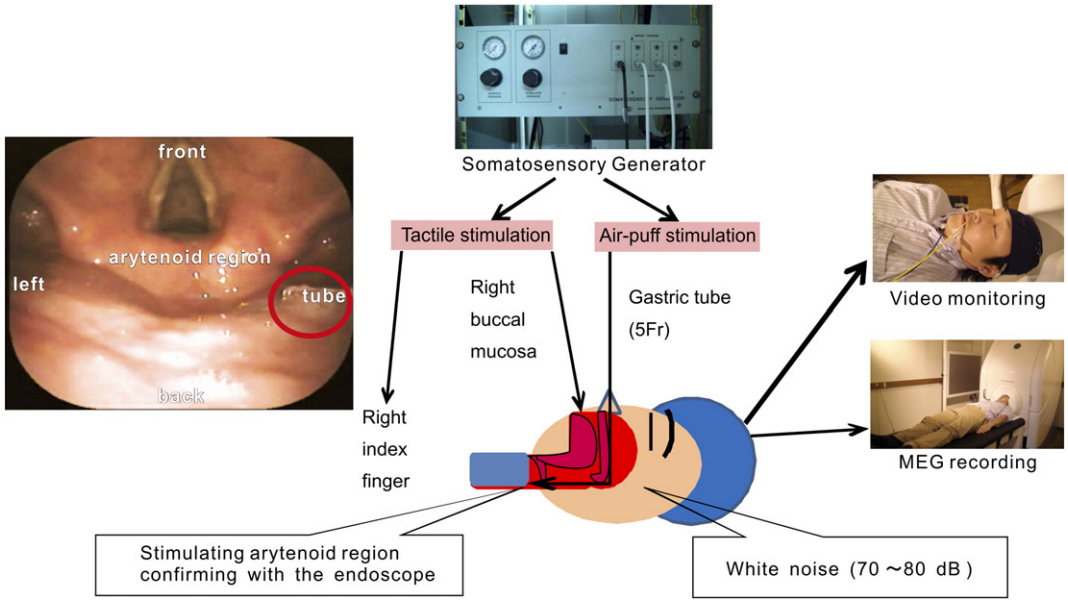

Fig. 1. A schematic view of the experimental configuration. *Stimulation*: A flexible laryngoscope was inserted into the nasal passage and the distal tip of the scope was advanced to confirm the location of the tip of a tube at the arytenoid region. The air pressure level was adjusted using a somatosensory generator. The right buccal mucosa and the right index finger were also stimulated with tactile stimulation. *Magnetoencephalography (MEG) recording and video monitoring*: Video monitoring was conducted to observe the subjects' behavior during the MEG measurements, the 2 modalities were synchronized using a trigger from the MEG acquisition setting.