Movement of the human upper airway during inspiration with and without inspiratory resistive loading

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Cheng S, Butler JE, Gandevia SC, Bilston LE. Movement of the human upper airway during inspiration with and without inspiratory resistive loading. J Appl Physiol 110: 69–75, 2011. First published October 21, 2010; doi:10.1152/japplphysiol.00413.2010.—The electromyographic (EMG) activity of human upper airway muscles, particularly the genioglossus, has been widely measured, but the relationship between EMG activity and physical movement of the airway muscles remains unclear. We aimed to measure the motion of the soft tissues surrounding the airway during normal and loaded inspiration on the basis of the hypothesis that this motion would be affected by the addition of resistance to breathing during inspiration. Tagged MR imaging of seven healthy subjects was performed in a 3-T scanner. Tagged 8.6-mm-spaced grids were used, and complementary spatial modulation of magnetization images were acquired beginning ~200 ms before inspiratory airflow. Deformation of tag line intersections was measured. The genioglossus moved anteriorly during normal and loaded inspiration, with less movement during loaded inspiration. The motion of tissues at the anterior border of the upper airway was nonuniform, with larger motions inferiorly. At the level of the soft palate, the lateral dimension of the airway decreased significantly during loaded inspiration (−0.15 ± 0.09 and −0.48 ± 0.09 mm during unloaded and loaded inspiration, respectively, P < 0.05). When resistance to inspiratory flow was added, genioglossus motion and lateral dimensions of the airway at the level of the soft palate decreased. Our results suggest that genioglossus motion begins early to dilate the airway prior to airflow and that inspiratory loading reduces the anterior motion of the genioglossus and increases the collapse of the lateral airway walls at the level of the soft palate.

Magnetic resonance tagging; magnetic resonance imaging; tagging; obstructive sleep apnea

Understanding how the upper airway collapses in sleep apnea may be important to improve treatments for the disorder. Measurements of electromyographic (EMG) activity of the upper airway muscles have identified the primary muscles that are involved in keeping the airway patent during respiration (18, 19, 26, 29, 30). However, the biomechanical mechanisms by which airway patency is maintained cannot be explained by those studies, as the presence of EMG activity does not indicate whether the muscle has shortened concentrically, remained isometric, or even lengthened eccentrically. Because of the complexity of the anatomic arrangements and the interaction between pharyngeal muscles, it is difficult to visualize how they alter the geometry of the airway dynamically during respiration.

Different imaging modalities (e.g., computerized tomography scans and MR imaging) have been used to measure changes in airway size during respiration in different regions of the airway (1, 6, 20, 31, 32). These studies show that airway size changes dynamically during respiration and indirectly demonstrate how the tissues surrounding the airway determine the airway patency with changes in intraluminal pressure. As a majority of these studies reported only the cross-sectional area (CSA) of the airway, details of changes in airway geometry (lateral vs. anteroposterior dimensions) and how the upper airway muscles and nearby tissues deform are not well understood. One of the imaging methods that can be used to study changes in airway geometry and deformation of airway muscles and nearby tissues is MR tagging (2, 4, 24, 25). In our previous MR tagging study (4), we showed that the genioglossus moved rhythmically with respiration. It contracts and moves anteriorly to dilate the airway during tidal inspiration in awake healthy subjects and posteriorly toward the end of inspiration and during expiration. However, one limitation of the study is that the timing of the anterior motion of the genioglossus in relation to inspiratory airflow was not accurately defined (see METHODS in Ref. 4).

The biomechanical response of the genioglossus and other soft tissues surrounding the upper airway at higher negative intraluminal pressure remains unclear. Although some studies have reported that the change in the upper airway’s lateral dimension is more prominent than the change in its anteroposterior dimension during inspiration (31, 34), little tissue motion was observed lateral to the airway in our previous work. We hypothesized that such movements would increase with higher negative intraluminal pressures. In addition, many studies have shown that genioglossus EMG activity at the multi-and single-unit level begins before airflow (9, 26, 27, 29, 33). Because of neuromuscular and biomechanical delays, it remains to be determined whether the mechanical motion of the genioglossus also precedes airflow. The present study was designed to compare the motion of the upper airway muscles and nearby tissues during normal breathing with that during inspiratory loaded breathing. We hypothesized that genioglossus motion decreases during inspiratory resistive loading and that lateral collapse of the upper airway at the level of the soft palate increases with higher negative intraluminal pressure. In addition, we also hypothesized that the genioglossus contracts and is likely to move anteriorly before inspiratory flow begins.

METHODS

Seven normal subjects (3 women and 4 men) with no history of sleep or other respiratory disorders volunteered for the study. Their mean age was 25.3 ± 2.6 (SD) yr, and body mass index (BMI) was 21.5 ± 2.7 kg/m². The study was approved by the Human Research Ethics Committee of the University of New South Wales and conducted according to the Declaration of Helsinki. Informed written consent was obtained from the subjects. All subjects had no contraindication for MR imaging.
Experimental Protocol

Subjects were required to breathe through a tight-fitting nose mask, which was connected to a low-resistance, two-way valve, so that inspiration occurred through a pneumotachometer (model 3700A, Hans Rudolph, Kansas City, MO) and pressure transducer (Tektronix, TDS 210, Portland, OR) located outside the MR scanner room (Fig. 1A). The inspiratory line was connected to the pneumotachometer and pressure transducer via 50- and 3-mm-diameter flexible tubes, respectively. Independent studies verified that there was no time lag between the pneumotachometer and the subjects. An inspiratory resistive load was applied by restriction of airflow at the pneumotachometer with a cylindrical plastic block (30 mm long) with a central hole (3 mm diameter). This induced a moderate inspiratory negative pressure (~4 cmH₂O) in the upper airway during quiet breathing. Preliminary experiments showed that when higher inspiratory loads were used, scanning was not successful, because tissues of the head and neck did not remain sufficiently still.

As the MR tagging technique is gated by the cardiac cycle, the MR imaging sequence requires a cardiac trigger pulse. The cardiac pulses were substituted by transistor-transistor logic (TTL) pulses generated using a LabVIEW program (version 8.2, National Instruments), and they were sent to the vector cardiogram input of the 3-T MR scanner (Achieva 1.2, Philips Medical Systems, Best, The Netherlands). TTL pulses at a frequency of ~1.3 Hz and mask pressure were monitored using a real-time digital oscilloscope (model TDS 210, Tektronix). Together with airflow recorded via the pneumotachometer, these signals were recorded continuously at 200 Hz using a data acquisition card (model VI6008, National Instruments) into a computer for subsequent analysis. To study the preinspiratory activation of the genioglossus, the scanner was triggered by a single TTL pulse timed so that the onset of inspiration occurred after the TTL pulse.

Scanning Protocol

Subjects were placed supine on the scanner bed and asked to keep still and breathe quietly. Pads were placed around the head to minimize head motion. We communicated with subjects by intercom to ensure that they were awake during scanning, and this was checked by verbal report after scanning sessions. Before the study, the scanner and the computer were synchronized to allow precise timing between scanner, trigger, and respiratory data.

Tags are applied by a magnetization preparation pulse prior to the actual imaging pulse sequence. The preparation pulse consists of a radio-frequency pulse and a strong gradient saturation pulse that saturates the longitudinal magnetization (24, 25). Two orthogonal sets of tags were generated over ~140 ms and appear as a square rectilinear grid formed by horizontal and vertical dark-colored tagged lines on the tissue image. The grids persist in the upper airway muscles throughout the scan and were used to track the motion of the soft tissues. A gradient echo pulse sequence was used for the actual imaging, and a total of eight tagged images were acquired. The MR parameters for the tagging sequence were as follows: 22 cm field of view, 2.1 ms repetition time, 0.9 ms echo time, 144 x 108 scan resolution, and 10 mm slice thickness. The overall scan repetition time, including the tagging and gradient echo acquisitions, was 2.14 s. Because of the need to manually line up the simulated cardiac pulses with the respiratory cycle, full data collection took ~1 h for each subject.

Images were taken in the midsagittal plane and in an axial plane in separate scanning series. The axial plane was defined by the tip of the soft palate as observed in the sagittal plane, chosen to determine tissue motion in the region of the soft palate. Scans were performed in each plane during normal inspiration and during inspiration with inspiratory resistive loading. Therefore, there were four scan series for each subject. The scanner was triggered prior to inspiratory airflow, and two to three repetitions were made in each series.

Data Analysis

Tags were tracked using the harmonic phase (HARP) method. Tissue motion was tracked by defining the coordinates of the points of interest on the undeformed tagged image, and the new locations of the
points in subsequent deformed tagged images were determined by the HARP method. The HARP method uses the principle that tissue deformation is directly related to the locations of the spectral peaks found in the tagged MR data in the Fourier domain, because changes in tag spacing alter the spatial frequency of the tagged grid. The program tracks the harmonic phase of the tagged grids and provides subpixel resolution, albeit by fitting a sinusoidal function (inherent in program tracks the harmonic phase of the tagged grids and provides interpolation. Although each pixel of the images is ~0.7–0.8 mm, depending on the imaging orientation, the HARP method has been shown to provide displacement errors of <0.1 pixel (11).

Motion of the genioglossus. The aim of the first analysis was to compare the motion of the genioglossus during normal and loaded inspiration. A point on the genioglossus (point A, Fig. 2A) was tracked at the level of the epiglottis on the midsagittal tagged images. This point was chosen to study genioglossus motion as genioglossus deformation and movement occur adjacent to the epiglottis and above the geniohyoid (4).

Movement of tissues along and adjacent to the airway. The aim of the second analysis was to analyze the motion of soft tissues at the anterior border of the upper airway during normal inspiration. On the midsagittal tagged images, a column of points (Fig. 2A) near the posterior border of the genioglossus was tracked at a distance of ~5 mm anterior to the airway periphery. The lowest point was at the level of the epiglottis (point A), and the highest point was at the level of the soft palate tip. The distance between each point was 5 mm.

Effects of negative pressure on upper airway tissue movement. The aim of the third analysis was to assess the effects of increased negative intraluminal pressure on movement of upper airway tissue at the level of the soft palate. A point (point D in Fig. 2B) was tracked ~10 mm anteriorly from the middle of the airway on the tagged images in the axial plane (see location of plane in Fig. 2A). In addition, two points (points B and C in Fig. 2B) ~5 mm adjacent and lateral to the airway were also tracked. The change in the airway’s lateral dimension was analyzed on the basis of the movement of points B and C. To allow comparison of data between the subjects during inspiration with and without resistive loading, the displacement of point D and the lateral change in airway dimensions at the soft palate were analyzed from 0% to 20% of inspiratory time.

Statistical Analysis

A paired t-test was used to compare the motion of point A during normal and loaded inspiration, the motion of point A before inspiratory flow during normal and loaded inspiration, and the change in the airway’s lateral dimension during normal and loaded inspiration. The significance of the linear regression for the motion of point D and the change in the airway’s lateral dimension during normal and loaded inspiration was also tested. All data are presented as means ± SE. Statistical significance was set at P < 0.05.

RESULTS

Genioglossus Movement During Normal and Loaded Inspiration

Figure 3A shows the displacement of point A in the genioglossus during normal and loaded inspiration in seven subjects. Positive and negative displacement represents the anterior and posterior motion of point A, respectively. The average mask pressure was ~1.9 ± 0.16 cmH₂O during normal inspiration and ~3.8 ± 0.23 cmH₂O during loaded inspiration. The displacement of point A over 10% of the inspiratory time during normal and loaded inspiration for all subjects is shown in Fig. 3C. The average displacement of point A during normal and loaded inspiration was 0.31 ± 0.04 and 0.10 ± 0.01 mm, respectively. A paired t-test showed that the anterior motion of point A was significantly higher (P < 0.05) during normal inspiration. [See movie clip MC 1 in Supplemental Material for this article, available online at the Journal website, which shows the difference in anterior motion of the genioglossus during normal and loaded inspiration (starting from 0% of inspiratory time) in 1 subject.] In five of seven subjects, there was at least one set of data with two measured positions of point A before inspiratory flow for normal and loaded inspiration (Fig. 3B). The average displacement of point A before inspiratory flow for these data was 0.34 ± 0.05 mm for normal inspiration and 0.20 ± 0.02 mm for loaded inspiration.

Tissue Movement Before and During Normal Inspiration Along and Adjacent to the Airway

Figure 4 shows the position of the selected points along the anterior border of the upper airway at 250-ms intervals during inspiration for all subjects in the midsagittal plane (Fig. 2A). During inspiration, the tissue movement was nonuniform along the length of the airway. In the majority of our subjects (subjects 1, 2, 3, 5, and 6), in the inferior half of the airway, most of the tissue motion was in the anterior direction, and tissue motion decreased superiorly (Fig. 4). The greatest anterior motion occurred at the lowest two points. In the superior half of the airway, tissue motion varied between subjects, and there appeared to be variable patterns of motion during inspi-
ration: tissue moved anteriorly to dilate the airway (subject 5); tissue moved posteriorly to narrow the airway (subjects 2, 3, and 7), or tissue in the superior section of the airway moved little (subjects 1, 4, and 6).

Tongue Movement in the Soft Palate Region During Inspiration With and Without Resistive Loading

Figure 5 shows the direction and magnitude of tissue motion for points C and D during normal (Fig. 5A) and loaded (Fig. 5B) inspiration. The average mask pressures during normal and loaded inspiration were $1.48 \pm 0.06$ and $3.01 \pm 0.16 \text{cmH}_2\text{O}$, respectively. During normal inspiration, the upper airway narrowed laterally ($0.15 \pm 0.09 \text{ mm}$). When the inspiratory resistive load was added, the upper airway narrowed laterally to a greater extent ($0.48 \pm 0.09 \text{ mm}$, $P < 0.05$). [See movie clip MC 2, which shows lateral narrowing of the airway in 1 subject, in Supplemental Material. During normal inspiration, the lateral collapse of the airway stops at 2 yellow lines superimposed on the airway; during inspiration with resistive loading, collapse of the airway exceeds the...
yellow lines. In some subjects, the change in the lateral dimension of the upper airway during inspiration with and without resistive loading was asymmetric. For example, the airway’s lateral dimension in some subjects decreased, with point B moving medially and point C moving laterally during inspiration. Figure 5C shows the change in the lateral dimension of the airway against the motion of point D. The data show that, during normal breathing, there is a relationship ($r^2 = 0.78$, $P < 0.03$) between the motion of point D (at the top of the airway) and the lateral dimension of the airway (distance between points B and C), such that anterior motion is associated with lateral narrowing of the airway and posterior motion of point D is associated with enlargement of the airway. During loaded inspiration, this relationship did not hold ($r^2 = 0.23$, $P < 0.03$), because those subjects who showed posterior motion of point D (in normal breathing) and lateral widening of the airway showed lateral narrowing associated with posterior motion of point D in loaded breathing.

**DISCUSSION**

This study shows that the genioglossus moves anteriorly during inspiration, and the anterior motion decreases during loaded inspiration. In five of seven subjects, a set of data showed that the genioglossus moved anteriorly before the start of inspiratory flow for normal and loaded inspiration. While the pattern of tissue deformation along the inferior half of the upper airway was similar (due to anterior motion of the genioglossus) in the majority of the subjects, it was more variable along the superior half of the airway. Unlike the genioglossus, soft tissue at the level of the soft palate (points B, C, and D) includes muscle fibers and passive soft tissues. Hence, tissue motion at this level will include contributions from both tissue types, so that it is influenced by contraction of muscles (genioglossus and stylohyoid) and intraluminal pressure (10). At the level of the soft palate, there was an inverse relationship between the change in the lateral and anteroposterior dimensions of the upper airway during normal inspiration. During mildly loaded inspiration, the inverse relationship was no longer significant, and lateral collapse of the upper airway increased. The lateral change in upper airway dimension is likely influenced by the passive deformation of the soft tissues around the airway (e.g., lateral fat pads) and the coactivation of other muscles during inspiration.

Increase in EMG activity in the genioglossus before inspiratory flow and during inspiration was demonstrated by single-unit (19, 30) and multiunit (28) studies. However, the mechanical effect of genioglossus EMG activity before inspiratory flow and during loaded inspiration has not been reported. This study shows that the genioglossus moves anteriorly before inspiratory flow (for normal and loaded inspiration), and this reflects the mechanical effect of respiratory drive to the muscle. Although we did not measure concurrent EMG activity while our subjects were in the scanner (because of MR technical constraints), EMG activity in the genioglossus is likely to increase with loaded inspiration (16, 26). This study shows that the movement of point A was greater during normal inspiration than during mildly loaded inspiration and suggests that the increase in EMG activity in the genioglossus during loaded inspiration.

**Fig. 5.** A: mean displacement of points B and C for 7 subjects during normal and loaded inspiration. △ and □ represent data from single breaths; horizontal gray bars represent average. Black arrows represent medial motion. B: inverse relationship between change in airway’s lateral dimension and anteroposterior motion of point D. Linear regression of relationship is high ($r^2 = 0.78$; △) during normal inspiration. Relationship is absent during inspiration with resistive loading ($r^2 = 0.23$; □).
inspiration does not act to dilate the airway further but, rather, acts to stiffen the airway.

In the midsagittal plane, tongue tissue along the upper airway moved variably in the anteroposterior direction and along the airway. Thus the size of the airway change is nonuniform along the airway during inspiration. While the inferior part of the genioglossus was moving anteriorly, tissue in the superior section of the airway moved posteriorly in some subjects \((n = 3)\) or anteriorly in others \((n = 2)\). This dynamic change in airway geometry may affect the effective moment-to-moment resistance at the level of the epiglottis during inspiration. The posterior motion of soft tissues in the superior section during inspiration is possible, as the human tongue appears to behave as a hydrostat \((7, 12)\), and its volume is conserved when the genioglossus contracts. In our previous study \((4)\), we showed that genioglossus activation (in the sagittal plane) could cause superior and inferior displacement of tissues above and below the muscle, respectively. The cranial displacement of soft tissues above the genioglossus can displace tissues posteriorly in the superior part of the tongue, as subjects were in a supine position. This motion of the tongue varies between subjects and is likely related to the anatomic differences in the airway, such as pharyngeal length \((17)\) and fat pads \((34)\).

Dynamic changes in airway caliber in the retropalatal region during inspiration have been studied by using different imaging modalities in normal subjects and patients with obstructive sleep apnea (OSA) \((3, 5, 6, 8, 20, 31, 32, 34)\). Most of these studies reported that the CSA of the airway was smallest during end expiration and/or during inspiration in awake nonsnorers and in OSA patients. Although we cannot analyze CSA (as the boundaries of the airway are obscured by the tags), the present study showed that, during inspiration, the change in airway caliber is associated with changes in lateral and anteroposterior airway lumen diameters. During loaded inspiration, this pattern of upper airway motion disappeared in some subjects (who showed posterior movement of the genioglossus) as the anteroposterior and lateral dimension of the upper airway decreases. Schwab and colleagues \((31)\) and Trudo and colleagues \((34)\) showed that a decrease in the lateral dimension of the airway is the predominant type of upper airway deformation at the level of the soft palate during inspiration. However, the lateral dimension of the airway increased during normal inspiration in four of our subjects. Nevertheless, the lateral airway dimension decreased during loaded inspiration for all subjects. In the study of Schwab and colleagues, the subjects had a higher average BMI than those in our study and, potentially, a higher tissue mass in the tongue. Thus it is possible that, in their subjects, the tongue would stiffen but would be incapable of moving anteriorly during inspiration, thus making the lateral walls of the upper airway more vulnerable to collapse.

There are several drawbacks in this study, and they were caused by the inherent limitations of the MR tagging technique. First, the temporal resolution of this technique maybe too low to image the preinspiratory activation of the genioglossus when a breath duration is short. Although all the scans were triggered before inspiration, in some data sets, there was only one data point for \(point A\) before inspiratory flow. In the majority of our data \((\sim 90\%)\), the first measured position of \(point A\) during inspiration was more anterior than the last measured position of \(point A\) before inspiratory flow. Although \(point A\) may not have necessarily moved anteriorly before the onset of inspiration, we believed that this is unlikely: in at least one set of data in six of seven subjects, there were two measured positions of \(point A\) before inspiration (for normal and loaded inspiration), and, in five of these subjects, there was anterior motion before inspiration. In addition, the temporal aspect of the anterior motion of \(point A\) before inspiration corresponded well with the results of Sabiosky and colleagues \((27, 29)\), who reported that the increase in EMG activity in the genioglossus begins at 5–30% of inspiratory time before inspiratory flow in healthy subjects.

Another inherent limitation of MR tagging is that data acquired using this technique are restricted to a short duration. Unlike other imaging techniques (e.g., endoscopy and ultrasound), tag fading limited our measurement of tissue deformation over a fraction of the respiratory cycle. Moreover, as we were motivated to study the preinspiratory activation of the genioglossus, we manually triggered the scanner before the onset of inspiration, based on monitoring the respiratory cycle. Although the respiration of our subjects was fairly consistent, there was some variability between breaths. For these reasons, measurements of the motion of soft tissues were commenced at different times before inspiratory flow in different subjects, and the measurements ended at different times during inspiration. For meaningful comparison of the magnitude of soft tissue motion between subjects, a fixed time span was chosen, and analysis was performed using only a portion of the data measured on the tongue and nearby structures. Lastly, although we used a 10-mm-thick image slice, this averaging should have little effect on our results, especially on images in the midsagittal plane, because the movement of regions across the width of the airway is rather uniform.

Despite the technical drawbacks of the MR tagging technique, measuring the dynamic motion of upper airway muscles with this technique is still important for several reasons. 1) With MR tagging, a detailed study of the motion of upper airway muscles with MR grids can be made \((2a)\). Without the grids, it can be difficult to identify the specific regions of muscle motion on an MR image. For example, activation of the genioglossus was believed to occur over the entire posterior section of the tongue. However, with the use of MR tagging, this study, along with our previous work, clearly shows that, in most subjects, genioglossus deformation occurs only at the inferior half of the tongue and is adjacent to the epiglottis (also see movie clip MC 1 in Supplemental Material). 2) MR tagging allows imaging in the sagittal plane, which is useful to study how patency of the upper airway is maintained by the tongue on a breath-to-breathe basis. Studying this by other imaging techniques (e.g., endoscopy and optical coherent tomography) may require analysis of the change in CSA at different levels of the upper airway, and this is not simple to do concurrently. This will require multiple measurements for several different breaths. 3) MR tagging allows study of the deformation of the upper airway muscles during respiration without the use of an invasive probe, such as an endoscope or the transducer of an ultrasound machine, which may physically alter the anatomic structure of the muscles surrounding the airway.

While the inherent biomechanical properties (e.g., tongue mass and stiffness) of the pharynx in OSA patients may be different from those of normal healthy subjects, the biome-
mechanics of how the upper airway collapses may be similar in both groups. This information has the potential to be used to examine the effectiveness of different treatments (e.g., mandibular advancement devices and functional electrical stimulation of upper airway muscles) for OSA (13–15, 21–23). The success of these therapies and treatments maybe enhanced by a better understanding of the movement of the muscles in the upper airway and the airway regions that are most vulnerable to collapse in an individual.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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