Tonic and Phasic Respiratory Drives to Human Genioglossus Motoneurons During Breathing

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Saboisky, Julian P., Jane E. Butler, Robert B. Fogel, Janet L. Taylor, John A. Trinder, David P. White, and Simon C. Gandevia. Tonic and phasic respiratory drives to human genioglossus motoneurons during breathing. J Neurophysiol 95: 2213–2221, 2006. First published November 23, 2005; doi:10.1152/jn.00940.2005. A tongue muscle, the genioglossus (GG), is important in maintaining pharyngeal airway patency. Previous recordings of multiunit electromyogram (EMG) suggest it is activated during inspiration in humans with some tonic activity in expiration. We recorded from populations of single motor units in GG in seven subjects during quiet breathing when awake. Ultrasonography assisted electrode placement. The activity of single units was separated into six classes based on a step-wise analysis of the discharge pattern. Phasic and tonic activities were analyzed statistically with the coefficient of determination ($r^2$) between discharge frequency and lung volume. Of the 110 motor units, 29% discharged tonically without phasic respiratory modulation (firing rate $\sim$ 19 Hz). Further, 16% of units increased their discharge during expiration (expiratory phasic and expiratory tonic units). Only half the units increased their discharge during inspiration (inspiratory phasic and inspiratory tonic units). Units firing tonically with an inspiratory increase had significantly higher discharge rates than those units that only fired phasically (peak rates 25 vs. 16 Hz, respectively). Simultaneous recordings of two or three motor units showed neighboring units with differing respiratory and tonic drives. Our results provide a classification and the first quantitative measures of human GG motor-unit behavior and suggest this activity results from a complex interaction of inspiratory, expiratory, and tonic drives at the hypoglossal motor nucleus. The presence of different drives to GG implies that complex premotor networks can differentially engage human hypoglossal motoneurons during respiration. This is unlike the ordered recruitment of motor units in limb and axial muscles.

INTRODUCTION

The neural control and biomechanical properties of the tongue are important factors in the pathophysiology of obstructive sleep apnea (Fogel et al. 2004; Malhotra and White 2002). The tongue is a muscular hydrostat that participates in diverse tasks such as swallowing, speech, and mastication. It helps maintain a patent airway during inspiration and expiration. This is vital especially during sleep when pharyngeal dilator muscle activity declines (Remmers et al. 1978). The output of brain stem respiratory oscillators varies with the sleep-wakefulness cycle (e.g., Peever et al. 2003) and also varies to the different respiratory motoneuron pools (e.g., Leiter and St. John 2004; cf. Onal et al. 1981).

The tongue comprises several “extrinsic” muscles (with origins outside the tongue) and “intrinsic” muscles (with origins and insertions within the tongue). Although the intrinsic tongue muscles can contract with respiration, they are usually inactive during quiet breathing (Bailey and Fregosi 2004). Hence most studies of neural control of human breathing have focused on the extrinsic muscle, genioglossus (GG), which originates from the inner surface of the lower jaw (Lowe 1980). Previous studies using multiunit intramuscular electromyographic (EMG) recordings have shown that GG is recruited phasically before and during inspiration and contracts tonically throughout expiration (e.g., Eastwood et al. 2003; Fogel et al. 2001; Sauerland and Harper 1976). However, it is not known if the same or different populations of motoneurons are involved. The GG is also reflexively modulated by input from pressure sensors in the upper airway (Akahoshi et al. 2001; Eastwood et al. 1999; Fogel et al. 2003; Horner et al. 1991a,b; Malhotra et al. 2000, 2002; Shea et al. 2000; Stanchina et al. 2002). Contraction of GG pulls the base of the tongue down and forward (Abd-El-Malek 1938; Brouillet and Thach 1979) and, together with other protruder muscles, enlarges the pharyngeal airway (Bailey and Fregosi 2003; Lowe 1980; Sokoloff 2000). Single motor-unit recordings have allowed us to identify the firing characteristics of motor units that can be formally classified into different groups. This was needed to determine how the overall pattern of GG activation during normal breathing is composed.

Maintenance of airway patency throughout the respiratory cycle requires sufficient output from hypoglossal motoneurons that innervate GG (Remmers et al. 1978). In the common condition of obstructive sleep apnea (Kim et al. 2004; Young et al. 1993), multiunit GG activity is increased when awake (Fogel et al. 2001; Mezzanotte et al. 1992; Remmers et al. 1978). With sleep onset, this neuromuscular compensation is impaired and can lead to airway obstruction (Wheatley et al. 1978). Although GG is an important upper airway dilator in sleep, little is known about the activity of single hypoglossal motoneurons innervating GG even in awake humans. In studies in cats, Hwang et al. (1983) and Withington-Wray et al. (1988) found hypoglossal motor axons were active either during inspiration or expiration, whereas others were active during both phases of respiration. It is unknown whether these axons projected to intrinsic or extrinsic muscles. In one study of a
small number of GG motor units in humans, Tsuiki and colleagues (2000) found units discharged during inspiration or both inspiration and expiration (see also Bailey et al. 2005; and in rats, John et al. 2005). However, no formal classification procedures were applied as used in other animal studies (Orem and Dick 1983). We hypothesized that there would be different populations of motoneurons with different firing properties that make up the overall pattern of human GG activity during respiration. To assess this, we adapted a method previously used to study neural drive to single motoneurons innervating inspiratory pump muscles, including the diaphragm (Gandevia et al. 1999). We determined the respiratory timing and discharge frequencies of a population of GG motor units. Our data suggest that the GG motoneuron pool receives a unique mix of inspiratory, expiratory, and tonic drives distributed differentially to the motoneurons and that individual motoneurons can receive a combination of different drives during the same respiratory cycle.

**Methods**

Studies were performed on seven healthy volunteers lying comfortably supine. Subjects gave informed written consent to the procedures which had been approved by the Human Research Ethics Committee of the University of New South Wales. The study conformed with the Declaration of Helsinki.

**Ultrasonography**

Before each study, the location and depth of the upper-airway musculature at the site of insertion of the electrode was assessed using real-time ultrasonography (model 128XP/4; Acuson, Mountain View, CA; Fig. 1A). The ultrasound transducer (7.5 MHz Acuson, linear probe) was positioned in a coronal plane 10–20 mm posterior to the mental protuberance. The distance from the skin to the inferior and superior margin of the GG and geniohyoid muscles and the lateral width of GG were recorded using an electronic caliper (Eastwood et al. 2003).

**General procedures**

Subjects breathed quietly through a sealed close-fitting nose mask with their mouth closed. The mask was connected via a two-way valve (Hans Rudolph, 1400, Kansas City, KS) with the inspiratory port connected to a pneumotachometer (Fig. 1B). The flow signal was integrated to give inspired volume. Respiratory movements of the chest and abdomen were recorded with calibrated inductance bands positioned around the thorax and the abdomen (Respitrace, Ardsley, NY). Subjects were asked to relax and breathe quietly and to remain awake throughout the procedure. Subjects occasionally swallowed, and this was readily detected and excluded from analysis.

**EMG recording**

The activity of single motor units (SMUs) innervating GG was recorded through a 26-gauge Teflon-coated monopolar needle electrode (50 mm in length with a recording area of 0.34 mm², Teca, Surrey, UK). A surface reference electrode was positioned ~30 mm from the needle over the left bony mandible. A large flexible ground was positioned on the right shoulder. About 1 h prior to recording, a local anesthetic cream (Emla, AstraZeneca) was applied to the skin to minimize any discomfort arising at the site of needle insertion. Needles were inserted ~10 mm posterior to the genial tubercle of the mandible and 3 mm from the midline on the left. Insertion was perpendicular to the skin surface to a depth of ~22–30 mm deter-
We estimate that the needle tip probably covered an arc of up to ∼3 cm within the muscle.

**Classification of SMUs**

Motor-unit potentials in the EMG signal were triggered from a threshold level determined for each site and activity of individual SMUs were sorted into “templates” based on their size and detailed morphology (Spike2 analysis system). Each individual motor unit potential was then inspected to check that it was correctly triggered. For each motor unit, instantaneous frequency plots were derived from the time of discharge of the unit. Each SMU was then classified into one of six types based on its pattern of discharge during the respiratory cycle as determined from the airflow signal (Fig. 2).

The units were classified with a strict three-step procedure based on off-line inspection of the pattern of each unit’s firing frequency and changes in inspiratory flow. First the units were classified into either tonic or phasic categories depending on whether they discharged throughout both inspiration and expiration, or predominantly during inspiration or expiration. To be designated as “tonic,” units had a minimal firing frequency that exceeded 2.0 Hz. Second, units were classified as inspiratory or expiratory if there was a reproducible peak in the firing frequency during inspiration or expiration (respectively). This gave four categories: inspiratory phasic units discharging phasically during inspiration, expiratory phasic units discharging phasically during expiration, inspiratory tonic units discharging through inspiration and expiration but with their peak frequency during inspiration, and expiratory tonic units discharging through inspiration and expiration but with their peak frequency during expiration. Finally, the residual tonically firing units that had no obvious respiratory or other modulation were classified as tonic. A small number of units remained that discharged variably, unrelated to inspiration or expiration, and they were classified as tonic other units. The robustness of the classification system was assessed (see Statistical analysis).

**Measurements of discharge properties**

The main measurements of discharge properties (see following text) were derived from the instantaneous frequency plot for each SMU over three consecutive normal breaths. The three breaths that were chosen had consistent respiratory timing and similar changes in inspiratory flow and volume. For inspiratory phasic, inspiratory tonic, and tonic units, measurements were made relative to the beginning of inspiration. For expiratory phasic and expiratory tonic units, measurements were made relative to the beginning of expiration. These time points were determined from integration of the inspiratory flow signal.

For phasic units, the onset discharge time was measured as the time at which the unit first began to discharge for each breath, and for inspiratory and expiratory tonic units onset time was taken at the time when the discharge frequency first increased above its tonic level (i.e., at the end of the shortened interspike interval). The end of respiratory discharges was determined with a similar procedure. The onset discharge frequency for the phasic units was calculated from the first interspike interval for each breath. For the inspiratory and expiratory tonic units, the onset firing frequency was measured at the first increase in the discharge frequency above the tonic level. The peak discharge frequencies were derived from the peak of the instantaneous frequency plot with a running average (smoothed over 200 ms) for each breath. The frequency of tonic units was also measured with a similar running average. The tonic other units were measured manually from the troughs and peaks of instantaneous frequency plots. The mean firing frequency and its SD were used to calculate the coefficient of variation for each unit. All variables were averaged for three typical consecutive breaths.

**Statistical analysis**

The discharge parameters of SMUs were assessed using a one-way ANOVA with Bonferroni post hoc analysis. If data were not normally distributed, then the Kruskal-Wallis test was applied. Differences in the behavior and distribution of the unit types were analyzed with Fisher’s exact and χ² tests. To assess unit categorization, each unit was checked independently by two observers, and the agreement between them was measured with the kappa statistic. In addition, cross-correlations between the signal of lung volume (from the inductance bands) and instantaneous firing frequency (smoothed over 200 ms) were computed for all possible phase differences between the two

![Fig. 2. GG motor-unit types. A–F, typical examples of the 6 types of motor-unit discharge recorded from GG during quiet breathing. The raw electromyograph (EMG), instantaneous discharge frequency plot for 1 unit derived from the raw signal and inspired volume are shown for each type of unit. Action potentials from the single units for 2 breaths are superimposed at the right of each panel. Vertical calibration bars for the EMG are 500 μV for A, B, and F and 200 μV for C–E, and the horizontal calibration bar is 2 ms. Recordings are from 3 different subjects; A and F, subject 1; B–D, subject 2; E, subject 7.](http://jn.physiology.org/)

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signals. The strength of each correlation was evaluated by calculating the linear coefficient of determination ($r^2$). The respiratory phase of the maximal $r^2$ determined whether the unit was classified as inspiratory or expiratory (see Orem and Dick 1983). Unless indicated in the text, values are given as the means ± SE. Statistical significance was set at $P < 0.05$.

**RESULTS**

The discharge of 110 SMUs was recorded from the GG during quiet breathing in seven subjects (5 males, 2 females; age: 42.9 ± 4.4 yr, height: 174.6 ± 1.9 cm; weight: 74.4 ± 3.4 kg; body mass index: 24.4 ± 1.0 kg/m$^2$, means ± SE) who were supine and awake. The mean number of units recorded from each subject was 16 (range: 11–22). Each unit was classified into one of six types based on its discharge characteristics and confirmed with cross-correlations of volume and smoothed firing frequencies. A typical example of each type is shown in Fig. 2.

**Ultrasound measurements**

To determine the depth and location for insertion of the electrode into GG the local anatomy of the upper airway musculature was examined with ultrasonography (Fig. 1). The mean distance from the skin to the inferior margin of the GG was 17.5 ± 3.0 mm and 27.6 ± 2.1 mm to the superior border of the GG. The mean width of the GG was 14.9 ± 1.3 mm. These values corresponded with measurements reported previously (Eastwood et al. 2003). The range in depth of needle insertion from the skin surface was ~22–30 mm determined from ultrasound (Fig. 1A).

**Classes of SMU activity in GG**

The SMUs were separated into six categories based on a three-step analysis of their firing characteristics: inspiratory phasic, inspiratory tonic, expiratory phasic, expiratory tonic, tonic, and tonic other (see METHODS). When assessed by two observers, the classification was concordant for 105 of the 110 units, i.e., for 95% of units (kappa = 0.94, $P < 0.001$). Another way to divide the units relied on the strength and timing of the peak coefficient of determination ($r^2$) between volume during quiet breathing and each unit’s discharge frequency. Data for all units are shown in Fig. 3, and the mean values for each class are given in Table 1. Tonic units usually showed low $r^2$ values (<0.4), whereas units with clear respiratory modulation had high $r^2$ values (>0.4). Inspiratory units had a peak $r^2$ before the end of inspiration (negative times) and expiratory units had a peak $r^2$ after the end of inspiration during expiration (positive times).

**TABLE 1.** Pooled peak coefficient of determination between the discharge frequency of units of each type and the respiratory volume

<table>
<thead>
<tr>
<th>Type of Unit</th>
<th>$r^2$</th>
<th>Lag Time, s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory phasic</td>
<td>0.63 ± 0.02</td>
<td>−1.46 ± 0.08</td>
</tr>
<tr>
<td>Inspiratory tonic</td>
<td>0.56 ± 0.03</td>
<td>−1.55 ± 0.32</td>
</tr>
<tr>
<td>Expiratory phasic</td>
<td>0.66 ± 0.04</td>
<td>2.27 ± 0.58</td>
</tr>
<tr>
<td>Expiratory tonic</td>
<td>0.60 ± 0.05</td>
<td>1.98 ± 0.41</td>
</tr>
<tr>
<td>Tonic</td>
<td>0.31 ± 0.02</td>
<td>0.34 ± 0.43</td>
</tr>
<tr>
<td>Tonic other</td>
<td>0.38 ± 0.05</td>
<td>0.74 ± 1.11</td>
</tr>
</tbody>
</table>

The timing of the peak correlation is given. Data are shown as means ± SE. Negative lag times correspond to inspiration and positive times to expiration.
discharge from onset to peak firing by 4.7 Hz, respectively, whereas the inspiratory and expiratory tonic units increased their discharge frequency from the background level by 8.2 ± 1.0 and 10.2 ± 1.0 Hz, respectively, almost twice as much as the units that showed only phasic activity (P < 0.05). The mean peak discharge frequency for (unmodulated) tonic units (19.5 ± 1.10 Hz) was higher, but not significantly, than that of inspiratory phasic units. Five units classed as tonic other increased their discharge frequency variably by 10.5 Hz (from 10.4 Hz at the trough to 20.8 Hz at the peak), but these changes were unrelated to respiration.

The distribution of motor unit types varied between subjects. Not all subjects showed evidence of each type (Table 2). However, in subjects 1 and 2, recordings were made from all six types, and tonic units and inspiratory phasic units were recorded from most subjects (6 of 7 subjects). The electrode was repositioned during each study to sample from different regions of the muscle in the anteroposterior plane (see Methods). Pooled data demonstrated an increased occurrence of units with tonic (75%) relative to phasic (25%) activity when sampling posteriorly in GG (P < 0.05). Similar proportions of tonic and phasic units were found in the anterior (53 vs. 47%) and middle regions (45 vs. 55%) of GG. No regional differences in distributions were observed for inspiratory versus expiratory units (P > 0.05).

Simultaneous motor unit recordings

Simultaneous recording of multiple-unit activity revealed that different types of units were located in close anatomical proximity within the muscle. There were 12 sites at which three units were recorded simultaneously through the same electrode. Two of these sites had the same type of activity in all units; in two sites, both inspiratory and expiratory activity were recorded and in five sites both phasic and unmodulated tonic activity were recorded. There were 23 sites at which two units were recorded simultaneously. Twelve of these sites had the same type of activity and at the remaining nine sites there were various combinations of unit activities.

Figure 6 shows two examples of two types of units being recorded concurrently. In Fig. 6A, the two units both discharged in phase with expiration, one an inspiratory tonic unit (unit 1) and the other an expiratory phasic unit (unit 2). After the third inspiration (at the arrow), the phasic unit stopped firing. This is presumably due to a decrease in expiratory drive as the unit resumed firing after the next (slightly larger) expiratory units.

![Fig. 4. Timing of discharge of GG motor units. The firing time for each motor unit (n = 105) during quiet breathing is shown relative to the phase of respiration (inspiration or expiration). For each unit, the dark horizontal lines represent the time that the discharge frequency increased with a phase of respiration, whereas the light horizontal lines represent the time that a motor unit discharged tonically. The phasic units are ordered within type according to the onset time of discharge relative to either the onset of inspiration or expiration. The tonic units were active throughout both inspiration and expiration and are separated between the phases to illustrate the total activity within the GG. Five tonic other units are not included.](image-url)

![Table 2. Number of units of the 6 types recorded in GG in each of the 7 subjects](table-url)

<table>
<thead>
<tr>
<th>Subject</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Total/Group</th>
<th>Percent of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiratory phasic</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>11</td>
<td>18</td>
<td>2</td>
<td>—</td>
<td>43</td>
<td>39.1</td>
</tr>
<tr>
<td>Inspiratory tonic</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>—</td>
<td>1</td>
<td>7</td>
<td>—</td>
<td>13</td>
<td>11.8</td>
</tr>
<tr>
<td>Expiratory phasic</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>Expiratory tonic</td>
<td>2</td>
<td>2</td>
<td>7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>12</td>
<td>10.9</td>
</tr>
<tr>
<td>Tonic</td>
<td>7</td>
<td>6</td>
<td>—</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>10</td>
<td>32</td>
<td>29.1</td>
</tr>
<tr>
<td>Tonic other</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>Total/subject</td>
<td>19</td>
<td>13</td>
<td>16</td>
<td>16</td>
<td>22</td>
<td>13</td>
<td>11</td>
<td>110</td>
<td>100</td>
</tr>
</tbody>
</table>

Distribution of motor unit types between and within individual subjects. Not all subjects showed evidence of each unit type. In total, 110 single motor units were studied.
inspiration. At the same time, the expiratory tonic unit also decreased its phasic firing during expiration. This example indicates that there is common phasic drive to both types of expiratory unit. Figure 6B shows an example of simultaneously recorded units receiving opposite respiratory drives. Unit 1 was active only in inspiration, and unit 2 was active only in expiration. This reflects differential inspiratory and expiratory drives to nearby motor units within GG.

**DISCUSSION**

This study provides the first detailed data on the recruitment times and discharge behavior of a large population of human GG motor units during normal breathing while awake and supine. It was possible to classify the activity of the 110 GG units reliably into six classes. Unit types with phasic inspiratory or expiratory modulation showed high peak correlations between discharge frequency and respiratory volume and the timing of the peak correlation occurred in the respiratory phase in which the peak discharge occurred (Orem and Dicke 1983).

Although widely regarded as an important dilator of the upper airway during inspiration (Remmers et al. 1978), 29% of the units discharged tonically at high rates (~20 Hz) with no respiratory modulation and 15% increased firing during expiration. Tonic units showed lower discharge variability than phasic types and were more commonly recorded posteriorly within GG. The current data suggest that the efferent neural drive to the GG most likely results from a combination of inspiratory, expiratory, and tonic drives.

**Different behavior of GG motor units**

Consistent with a role in maintaining upper airway patency, about half the GG units increased their discharge during inspiration. In addition, about a quarter of inspiratory phasic units discharged before inspiratory flow began and the remainder began to discharge early in inspiration. Inspiratory phasic units usually stopped firing well before the end of inspiration. Similarly, most inspiratory tonic units increased their discharge before or early in inspiration and usually maintained this throughout inspiration. The early firing of inspiratory phasic and inspiratory tonic units prior to inspiratory airflow indicates that the respiratory-related neural drive is not purely reflex (in response to negative airway pressure) because it begins before any negative pressure is generated by the respiratory pump muscles. Preinspiratory phasic activity of the upper airway dilator muscles can be inhibited when central respiratory drive is removed by mechanical ventilation (Akahoshi et al. 2001;
The tendency for the inspiratory phasic units to stop discharging well before the end of inspiratory flow may reflect a combination of decreased central inspiratory drive and decreased reflex support as negative airway pressure declines.

The timing of the discharge of inspiratory phasic GG motor units is different from that of motor units innervating inspiratory pump muscles such as the diaphragm and scalenes, which act on the chest wall. Although a few of their units discharge before the onset of flow, there is progressive recruitment of new units throughout inspiration. Furthermore, once recruited, most of these units discharge throughout inspiration and early into expiration (Butler et al. 2001; De Troyer et al. 2003; Gandevia et al. 1999; Saboisky et al. 2004).

During expiration, positive airway pressure acts to maintain expiratory flow and keep the upper airway open. Nevertheless, we found some expiratory activity in the GG. The expiratory phasic and expiratory tonic GG motor-unit activity recorded in the current study has not been previously reported in humans, although recordings from hypoglossal nerve fibers in the cat have shown expiratory activity (Hwang et al. 1983; Mitra and Cherniack 1983; Sica et al. 1984; Withington-Wray et al. 1988).

The role of expiratory units is presumably to stiffen the upper airway, particularly late in expiration, when upper airway collapse usually occurs (Badr 1996). At one site in GG, we simultaneously recorded activity from an inspiratory phasic and an expiratory phasic unit. As their activity was recorded with one electrode, such units are likely to be located in close proximity within the muscle. Although, the units were active in opposite respiratory phases, they probably do not have opposite mechanical actions. Stimulation of the medial branch of the hypoglossal nerve that innervates GG will protrude the tongue (Abd-El-Malek 1938; Eisele et al. 1997; Smith et al. 1996), and we hypothesize that both inspiratory and expiratory GG motor units lead to tongue protrusion. However, the mechanical action of the different classes of GG motor units is not known. We note the variability between subjects in the distribution of the different classes of units. This may be related to anatomical features of the upper airway and the required neural activation of the muscles in individual subjects.

The firing rates of tonic units were typically higher than firing rates for the phasic units. Thus the onset discharge frequency of the inspiratory tonic units and the mean discharge rate of tonic units were significantly higher than the onset discharge frequency of inspiratory phasic units (16.5 and 19.5 vs. 10.3 Hz). Similarly, the peak discharge frequencies of the inspiratory tonic motor units were higher than the inspiratory phasic units (24.7 vs. 15.0 Hz). The expiratory tonic motor units also reached higher peak rates than both the expiratory phasic and inspiratory phasic units. Furthermore, the modulation of discharge frequency was also significantly greater for the inspiratory tonic and expiratory tonic units compared with inspiratory phasic and expiratory phasic units. This implies that the motoneurons with modulated tonic discharges are either responding differently to the same respiratory drive or are receiving an additional respiratory drive. The motor unit firing frequencies (onset and peak) for the GG are also high when compared with inspiratory pump muscles, even for inspiratory phasic and expiratory phasic GG units (Butler et al. 2001; De Troyer et al. 2003; Gandevia et al. 1999; Saboisky et al. 2004).

Although this may be because the GG motor units have fast twitch times (Hellstrand 1981; van Lunteren and Manubay 1992), the relationship between force and stimulus frequency for diaphragm and GG is almost overlapping for a range physiological firing rates (van Lunteren and Manubay 1992). The level of contraction of the GG during normal breathing is low compared with a weak tongue protrusion and only ~6% of the activity during a large swallow (Akahoshi et al. 2001). Thus the high firing rates of GG motor units do not necessarily reflect a very high level of muscle contraction.

Neural drive

The output of the GG component of the hypoglossal motor nucleus appears to show six types of activity. Can this be explained by different thresholds within a single motoneuron pool? We think this is unlikely for the following reasons. First, there are separate phasic inspiratory and expiratory units. Second, some of the motoneurons that are already firing tonically, and therefore already at threshold, do not increase their discharge until late in a respiratory phase rather than at the beginning. This suggests that the respiratory drive to the motoneuron is separate from the tonic activity but combined in the output of the motoneuron. The types of motor-unit activity could be produced by variable combinations of three types of premotor drive: inspiratory, expiratory, and tonic. Some motoneurons are active tonically and do not receive phasic inspiratory or expiratory drives. Such motoneurons may be unaffected by reflex inputs from the upper airway, responsible for modulation of the multiunit EMG (Akahoshi et al. 2001). Other tonically active motoneurons respond to phasic drive by increasing their discharge frequency during inspiration or expiration, while some motoneurons appear to receive only phasic inspiratory or expiratory drive.

The high firing frequencies of inspiratory tonic and expiratory tonic units may be due to a phasic respiratory drive superimposed on tonic drive. Despite recording under controlled conditions, we found examples of differentially distributed drive to GG motoneurons. Figure 6A indicates that there may be common phasic drive to simultaneously recorded units but a differential tonic drive, whereas Fig. 6B shows differential drive (inspiratory and expiratory) to motoneurons. These were not isolated observations and were made while recording through a single electrode. Thus the motor units are likely to be in close proximity in the muscle. Recording from the hypoglossal nerve fibers in decerebrate cats also shows combinations of activity with fibers discharging through inspiration or expiration, as well as tonically (Hwang et al. 1983). Our data suggest that similar patterns of activation occur in human GG motor units.

Two features of the discharge behavior of GG motoneurons deserve comment. First, the discharge frequency of some motoneurons that fired tonically in a cyclical manner failed to be modulated by respiration when the overall output from the motoneuron pool increased. Second, there were subgroups of motoneurons activated in the inspiratory or expiratory phase of the cycle. These discharge characteristics contrast with the behavior of motoneuron pools innervating limb and trunk muscles (Henneman 1957; for review, see Binder et al. 1996; Burke 1981), and inspiratory pump muscles (Gandevia et al. 1999). The multiple motoneuron discharge patterns presum-
ably act to ensure airway patency during quiet breathing while still allowing flexible control of the tongue for its other functions such as eating and speaking.

In summary, this is the most complete description of human GG motor-unit activity to date. A classification system, backed up with a correlation analysis, is proposed to describe the different types of activity encountered. Such data are essential before more detailed studies are conducted on state-dependent, regional, and disease-related changes in human GG behavior. We have evidence for complex interactions affecting the output of upper airway motoneurons, and we propose that they are organized to overcome the collapsible airway and to allow the tongue to perform its range of important tasks.

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