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Collapsibility of the Upper Airway at Different Concentrations of Propofol Anesthesia

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Background: **This study investigated the effect of varying concentrations of propofol on upper airway collapsibility and the mechanisms responsible for it.**

Methods: **Upper airway collapsibility was determined from pressure–flow relations at three concentrations of propofol anesthesia (effect site concentration = 2.5, 4.0, and 6.0 μg/ml) in 12 subjects spontaneously breathing on continuous positive airway pressure. At each level of anesthesia, mask pressure was transiently reduced from a pressure sufficient to abolish inspiratory flow limitation (maintenance pressure = 12 ± 1 cm H_2O) to pressures resulting in variable degrees of flow limitation. The relation between mask pressure and maximal inspiratory flow was determined, and the critical pressure at which the airway occluded was recorded. Electromyographic activity of the genioglossus muscle (EMGgg) was obtained *via* intramuscular electrodes in 8 subjects.**

Results: **With increasing depth of anesthesia, (1) critical closing pressure progressively increased (−0.3 ± 3.5, 0.5 ± 3.7, and 1.4 ± 3.5 cm H_2O at propofol concentrations of 2.5, 4.0, and 6.0 μg/ml respectively; $P < 0.05$ between each level), indicating a more collapsible upper airway; (2) inspiratory flow at the maintenance pressure significantly decreased; and (3) respiration-related phasic changes in EMGgg at the maintenance pressure decreased from 7.3 ± 9.9% of maximum at 2.5 μg/ml to 0.8 ± 0.5% of maximum at 6.0 μg/ml, whereas tonic EMGgg was unchanged. Relative to the levels of phasic and tonic EMGgg at the maintenance pressure immediately before a decrease in mask pressure, tonic activity tended to increase over the course of five flow-limited breaths at a propofol concentration of 2.5 μg/ml but not at propofol concentrations of 4.0 and 6.0 μg/ml, whereas phasic EMGgg was unchanged.**

Conclusions: **Increasing depth of propofol anesthesia is associated with increased collapsibility of the upper airway. This was associated with profound inhibition of genioglossus muscle activity. This dose-related inhibition seems to be the combined result of depression of central respiratory output to upper airway dilator muscles and of upper airway reflexes.**

This article is accompanied by an Editorial View. Please see: Litman R: Upper airway collapsibility: An emerging paradigm for measuring the safety of anesthetic and sedative agents. ANESTHESIOLOGY 2005; 103:453–4.

PROPOFOL is a versatile anesthetic agent that is commonly used for induction and maintenance of anesthesia and, in lower doses, for sedation. Propofol sedation is often used for minor procedures, such as endoscopy, where the upper airway may be relatively unprotected. Maintenance of airway patency is a primary consideration under these circumstances and may depend, at least in part, on persisting upper airway muscle activity at sedating concentrations of propofol. Although general anesthetic agents are thought to exhibit dose-dependent attenuations of upper airway muscle activity,[1–6] this relation has not been examined in detail for propofol. This information is important because vulnerability to collapse of the upper airway is likely to increase with any dose-related decrease in pharyngeal dilator muscle activity. Understanding the nature of the relation is fundamental to the safe use of propofol in settings where upper airway patency is at risk.

There have been few previous studies of the dose-dependent depression of upper airway muscle activity by general anesthesia in humans,[5] with most information derived from animal studies.[1–4] The only previous study that has directly related decreases in upper airway muscle activity to changes in collapsibility in humans was undertaken by our group using isoflurane, where we demonstrated profound effects on both even at light planes of anesthesia.[6] Because propofol has a flatter dose–clinical response relation with a wider range of intensity of effect from sedation to anesthesia, it might also be expected to exhibit a more graduated effect on upper airway muscle activity.

The purpose of this study was to determine the effect of varying concentrations of propofol on upper airway collapsibility and the mechanisms responsible for it. In the latter regard, we sought to identify the effects of anesthesia on central respiratory drive to upper airway dilator muscles and its effects on upper airway reflexes.[7] A further aim of the study was to determine whether a sufficient dose of propofol could produce complete flaccidity of the upper airway and thereby provide suitable conditions for study of the mechanical behavior of the upper airway devoid of neurogenic influences. Apart from its implications for anesthesia, our previous work suggests that such conditions could also be used to determine vulnerability to obstruction during the relative atonia of sleep, particularly rapid eye movement sleep.[8]

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Materials and Methods

Subject Selection

Twelve subjects were recruited from those undergoing minor surgical procedures not involving the head or neck. All were white. Recruitment was independent of any known vulnerability to upper airway collapse (*e.g.*, obesity, snoring). Informed consent was obtained in writing from each subject before participation. The study was approved by the Sir Charles Gairdner Hospital Human Research Ethics Committee (Nedlands, Western Australia, Australia).

Subject Preparation

No premedication was administered. Standard monitoring was applied, and a vein cannulated. Sedation/anesthesia was induced with intravenous propofol (Diprivan; Astra Zeneca, Alderley Park, Cheshire, United Kingdom), administered *via* a Diprifusor (Astra Zeneca) target-controlled infusion system (Graseby 3500; SIMS Graseby, Watford, United Kingdom), which calculated effect site concentration on the basis of a three-compartment pharmacokinetic algorithm.[9,10] At a subanesthetic concentration of propofol (calculated effect site concentration of approximately 1.0 μg/ml), intramuscular electrodes were inserted percutaneously to measure genioglossus electromyogram (EMGgg).[11,12] Two 25-gauge needles, each containing two sterile 50-μm nylon-coated stainless steel fine-wire electrodes (Stablohm 800B; California Fine Wire Company, Grover Beach, CA), were inserted 1.0 cm from the symphysis menti to a depth of approximately 25 mm. Each needle was inserted approximately 0.3 cm lateral to the midline, angled slightly anteriorly toward the mandible so as to position the recording electrodes close to the origin of the genioglossus. Once in position, the needle was withdrawn, leaving the recording wires behind. The two pairs of bipolar wire electrodes were referenced to a common ground, placed on the forehead. In addition, a bipolar pair was derived from a single wire from each pair, thereby providing a third EMGgg signal. Each EMGgg signal was amplified, band-pass filtered (10–3,000 Hz, model 7P3; Grass Instruments, West Warwick, RI), full-wave rectified, and processed with leaky integrators with a time constant of 100 ms to yield a moving-time-averaged EMGgg on which later analyses were performed. As soon as the recording wires were connected, the subject was asked to voluntarily protrude the tongue and swallow. When satisfactory signals were collected, the propofol target blood concentration was increased to 6.0 μg/ml.

As consciousness was lost with increasing propofol concentration the subject was fitted with a chin strap, the mouth was taped, and a tight-fitting nasal mask was applied *via* which oxygen was delivered with a Bain circuit (fresh gas flow rate ≥ 14 l/min). Connected in series to this circuit was an expiratory port and a bilevel positive pressure source (BiPAP; Respironics, Murraysville, PA). This permitted a continuous positive airway pressure (CPAP) to be maintained using the device's inspiratory positive airway pressure mode. Also, airway pressure could be abruptly reduced to a preset lower level by switching to the ventilator's expiratory positive airway pressure mode on which this level was set.[6] Alternatively, a preset subatmospheric pressure could be rapidly applied by switching to a regulated vacuum source (model VFC204P; Fuji Electric Co., Tokyo, Japan). Airflow was monitored with a pneumotachograph (Hewlett Packard 47303A; Waltham, MA) that had been calibrated with four known flows using flowmeters. Nasal mask pressure (Pm) was measured *via* a port in the mask by a pressure transducer (model 143PC, Micro Switch; Honeywell, Morristown, NJ). Before each study, the transducer was calibrated with five known pressures. Once the nasal mask had been fitted, the mouth was occluded by adhesive tape, the head was carefully placed in a neutral position with lower cervical flexion and upper cervical extension (using a Shea headrest), and a maintenance CPAP level that was sufficient to abolish inspiratory flow limitation was applied.[13,14]

In seven subjects, the Bispectral Index was also derived from the frontal electroencephalogram and calculated by the A-2000 BIS® monitor using the four BIS® sensor electrodes (Aspect Medical Systems, Newton, MA).

All signals were digitally recorded continuously at 1,000 Hz on a PowerLab data acquisition and analysis system (model 16s; ADInstruments, Sydney, Australia).

Protocol for Assessment of Upper Airway Function during General Anesthesia

When a propofol effect site concentration of 6.0 μg/ml was obtained and stable ventilation was established, airway pressure was rapidly changed (during early expiration) from the maintenance level to a lower pressure for five successive breaths before being changed back to the maintenance level (immediately after the fifth inspiratory effort). After a recovery period, this procedure was repeated at a range of positive and, where necessary, negative airway pressures to produce variable degrees of inspiratory flow limitation (fig. 1). The order of application of pressures was randomized. When a sufficient number of measurements had been obtained, the target blood concentration was decreased to 4.0 μg/ml. Measurements were repeated when an effect site concentration of 4.0 μg/ml was achieved. Finally, the target blood concentration was again decreased, and measurements were repeated at an effect site concentration of 2.5 μg/ml.

Immediately after measurements at 2.5 μg/ml, the target blood concentration was increased, the nasal mask and EMGgg electrodes were removed, a laryngeal mask (*LMA-Classic*™; Pacific Medical, Victoria, Australia) was inserted, and the subject was prepared for surgery.

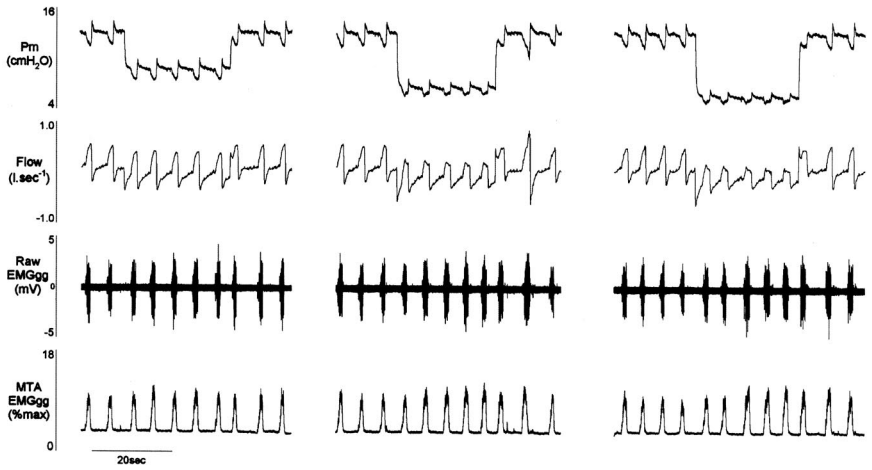

Fig. 1. Polygraph example from one subject (No. 6) of the changes in mouth pressure (Pm), flow, and raw and moving-time-averaged (MTA) genioglossus electromyogram (EMGgg) at a propofol effect site concentration of 4.0 μg/ml. Pm was variably decreased for five breaths from maintenance pressure of 13 cm H_2O to pressures sufficient to cause inspiratory flow limitation.

Data Collection and Analysis

At each level of anesthesia, upper airway pressure–flow relations were derived as previously described for sleeping and anesthetized subjects.[8,13–16] Briefly, with each reduction in Pm, the inspiratory flow (Vi) profile was examined for each of the five consecutive breaths. A plateau in the shape of the inspiratory flow profile was considered to be indicative of flow limitation.[17] For these flow-limited breaths, maximum inspiratory flow (Vi_{max}) and Pm were averaged over breaths 3–5 of each sequence at each of the three levels of anesthesia. The relation between Vi_{max} and Pm was examined, and the least squares linear regression equation computed at each level of anesthesia. The regression equation was then solved for Pcrit (the Pm at which Vi_{max} became zero). Resistance of the upper airway upstream of the site of pharyngeal collapse was calculated as the reciprocal of the slope of the regression equation.[13] Measurements of peak inspiratory and expiratory amplitudes of the moving-time-averaged EMGgg signal, relative to electrical zero, were obtained during breaths at the maintenance pressure, during breaths when Pm was reduced from the maintenance pressure, and during voluntary tongue protrusions and swallows. Tonic activity was defined as the difference between electrical zero and end-expiratory activity. Phasic activity was defined as the difference between end-expiratory and peak-inspiratory activity. Measurements were expressed as a percent change from the maximal value obtained during voluntary tongue protrusions and swallows.

Statistical Analyses

Comparisons of each variable at each level of anesthesia were undertaken using one-way repeated-measures analysis of variance. A Holm-Sidak *post hoc* test was applied when significant differences were detected. When data were not normally distributed, comparisons were undertaken using a one-way repeated-measures analysis of variance on ranks. In this circumstance, a Tukey *post hoc* test was applied when significant differences were detected. A value of $P < 0.05$ was considered significant. All values are represented as mean ± SD, except for box and whisker plots, which include the median, 5th, 25th, 75th, and 95th percentiles.

Results

A total of 12 subjects, 11 men and 1 woman, participated in the study. Anthropometric data are presented in table 1. Measurements of upper airway collapsibility were obtained in all subjects at 2.5, 4.0, and 6.0 μg/ml. EMGgg measurements were obtained in 8 subjects. Bispectral Index measurements were obtained in 7 subjects.

For the group, a Pm of 12 ± 1 cm H_2O was sufficient to maintain airway patency and abolish inspiratory flow limitation. At each level of anesthesia, Vi_{max} was linearly related to Pm for flow-limited breaths (mean r^2 for all subjects = 0.92 ± 0.08, 0.97 ± 0.02, and 0.96 ± 0.03 at propofol concentrations of 2.5, 4.0, and 6.0 μg/ml, respectively). This relation is shown for one subject in figure 2. The pressure at which flow became zero, Pcrit, progressively increased with increasing depth of anesthesia (−0.3 ± 3.5, 0.5 ± 3.7, and 1.4 ± 3.5 cm H_2O at propofol concentrations of 2.5, 4.0, and 6.0 μg/ml, respectively; $P < 0.05$ between each level), indicating a more collapsible upper airway (fig. 3). Resistance upstream to the site of collapse was unaffected by depth of anesthesia (13.9 ± 4.3, 13.7 ± 4.7, and 15.5 ± 6.4 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ at propofol concentrations of 2.5, 4.0, and 6.0 μg/ml, respectively; $P > 0.05$). BIS and maximum inspiratory flow at the maintenance pressure significantly decreased with increasing depth of anesthesia (fig. 3).

At subanesthetic concentrations of propofol (calculated effect site concentration of approximately 1.0 μg/ml), respiration-related phasic changes in EMGgg activity were observed in all eight subjects in whom it was measured. When breathing *via* the nasal mask at the maintenance pressure, respiration-related phasic changes in EMGgg activity were observed in 8 of 8, 7 of

Table 1. Anthropometric Data and Upper Airway Collapsibility

Subject No.	Sex	Age, yr	Height, cm	Weight, kg	BMI, kg/m^2	Pcrit, cm H_2O, during Propofol Anesthesia at 2.5 μg/ml	4 μg/ml	6 μg/ml
1	M	30	155	85	35	3.0	3.5	3.4
2	M	24	170	78	27	−2.4	0.1	1.7
3	M	49	175	86	28	−2.3	−2.1	1.5
4	M	46	177	83	26	0.2	1.9	1.9
5	M	49	178	85	27	4.8	5.7	5.7
6	M	52	175	81	26	2.7	2.8	3.6
7	M	32	180	89	27	5.2	6.4	6.8
8	F	50	164	88	33	−3.9	−3.6	−2.9
9	M	29	176	83	27	−4.6	−4.2	−3.9
10	M	23	186	84	24	−0.4	−0.9	0.6
11	M	47	178	90	28	−1.0	1.4	2.2
12	M	29	180	85	26	−4.7	−4.6	−4.3
Mean		38	175	85	28	−0.3	0.5	1.4
SD		11	8	3	3	3.5	3.7	3.5

Measures of upper airway collapsibility (Pcrit) were obtained at three concentrations of propofol anesthesia (effect site concentrations 2.5, 4.0, and 6.0 μg/ml). BMI = body mass index.

8, and 4 of 8 subjects at propofol concentrations of 2.5, 4.0, and 6.0 μg/ml, respectively. A representative polygraph example from one subject of the effect of propofol on EMGgg is shown in figure 4. For the group, the magnitude of phasic activity progressively decreased with increasing depth of anesthesia, being 11.0 ± 6.0% of maximum at a propofol concentration of approximately 1.0 μg/ml and 0.8 ± 0.5% of maximum at a propofol concentration of 6.0 μg/ml (fig. 5). Tonic activity was unchanged by depth of anesthesia, being 4.7 ± 1.6% of maximum at a propofol concentration of approximately 1.0 μg/ml and 3.9 ± 4.8% of maximum at a propofol concentration of 6.0 μg/ml (fig. 5).

For each subject, at each level of anesthesia, changes in phasic and tonic EMGgg were analyzed for each breath when airway pressure was decreased to close to Pcrit (*i.e.*, presence of marked flow limitation without complete airway collapse). These analyses showed that, relative to the level of phasic activity at the maintenance pressure immediately before the pressure decrease, phasic activity did not change over the course of the five breaths, regardless of level of anesthesia (fig. 6). Relative to the level of tonic activity at the maintenance pressure immediately before the pressure decrease, tonic activity tended to increase over the course of the five breaths at

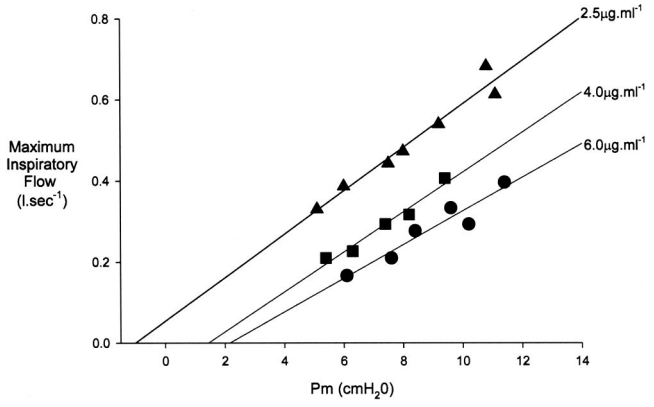

Fig. 2. Pressure–flow relation generated in one subject (No. 11) at propofol effect site concentrations of 2.5 (*triangles*), 4.0 (*squares*), and 6.0 mg/ml (*circles*). Pm = mask pressure.

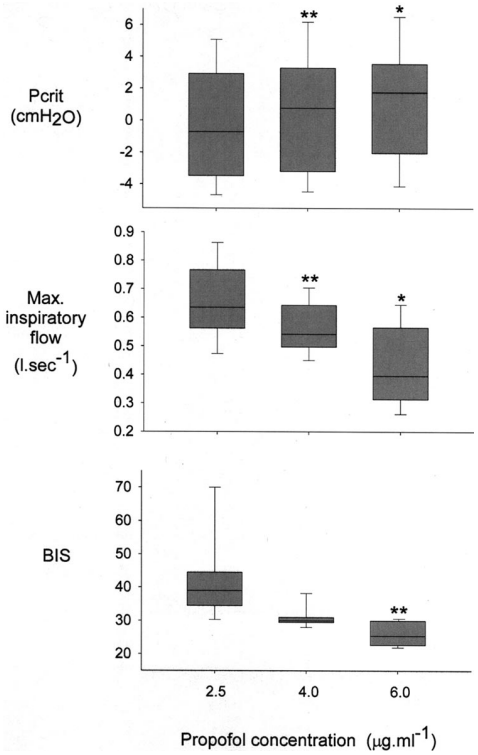

Fig. 3. Effect of anesthetic depth on upper airway collapsibility (Pcrit; n = 12), maximum inspiratory flow while breathing at the maintenance pressure (n = 12), and Bispectral Index (BIS; n = 7). Results are expressed as box and whisker plots, including median, 5th, 25th, 75th, and 95th percentiles. * $P < 0.05$ *versus* 4.0 and 2.5 μg/ml propofol. ** $P < 0.05$ *versus* 2.5 mg/ml propofol.

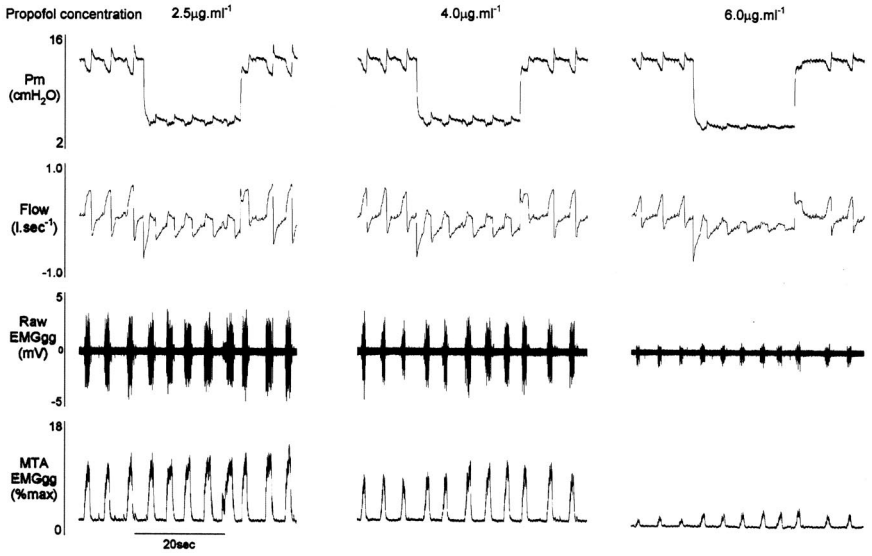

Fig. 4. Polygraph example from one subject (No. 6) of changes in mouth pressure (Pm), flow, and raw and moving-time-averaged (MTA) genioglossus electromyogram (EMGgg) at propofol effect site concentrations of 2.5, 4.0, and 6.0 μg/ml. At each level of anesthesia, Pm was decreased from a maintenance pressure of 13 cm H_2O to a pressure of approximately 5 cm H_2O. The degree of inspiratory flow limitation was greatest at a propofol concentration of 6.0 μg/ml.

a propofol concentration of 2.5 μg/ml but not at propofol concentrations of 4.0 and 6.0 μg/ml (fig. 6).

Discussion

This study examined the effect of increasing depth of propofol anesthesia on the neuromechanical behavior of the human upper airway. The major findings of the study were (1) that the propensity for the upper airway to collapse increased with increasing depth of propofol anesthesia in a dose-dependent fashion and (2) that this increased collapsibility was accompanied by a progressive decrease in phasic inspiratory activity of the genioglossus muscle and in reflex responsiveness of the genioglossus to collapsing forces, particularly at deeper levels of anesthesia.

Effect of Anesthetic Depth of Upper Airway Collapsibility

At each of three levels of propofol anesthesia, we varied airway pressure to induce variable degrees of inspiratory flow limitation and then examined the relation between pressure and flow to determine the pressure at which the pharynx occluded (no inspiratory flow).[8,13–16] This "critical pressure" (Pcrit) describes the propensity for the upper airway to collapse such that an airway that is resistant to collapse will require a negative pressure to occlude it (a negative Pcrit), whereas a very flaccid airway will obstruct at greater pressures (a positive Pcrit).

In the current study, Pcrit progressively increased as anesthetic depth increased, from -0.3 ± 3.5 cm H_2O at 2.5 μg/ml to 1.4 ± 3.5 cm H_2O at 6.0 μg/ml (fig. 3). Although the range of values of Pcrit was similar to those we recently reported with increasing anesthetic depth using isoflurane,[6,8] the change with increasing depth was more graduated. Increases in the depth of anesthesia were not associated with alterations in resistance of the upper airway upstream of the site of pharyngeal collapse, indicating that this part of the airway was not involved in the modulation of Vi_{max}. It is therefore likely that, in the flow-limited state, the responses in Vi_{max} (to anesthesia) were primarily due to changes in Pcrit, representing alterations in pharyngeal collapsibility. Such a conclusion is consistent with studies of upper airway morphology using magnetic resonance imaging, which show that propofol decreases upper airway size in adults and children.[18,19] Although measures of pharyngeal function were not undertaken in those studies, the anesthesia-induced changes in upper airway geometry reflect a more obstruction-prone pharynx, as indicated by our findings.

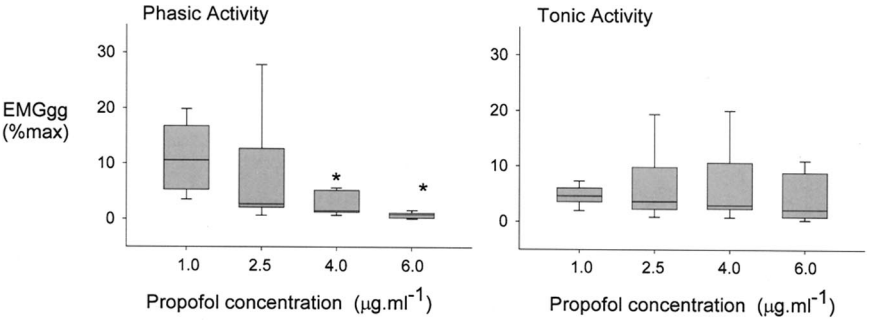

Fig. 5. Effect of anesthetic depth on the amplitude of phasic and tonic genioglossus electromyogram (EMGgg) activity while subjects were breathing at a maintenance pressure (*i.e.*, no evidence of inspiratory flow limitation). Results are expressed as box and whisker plots, including median, 5th, 25th, 75th, and 95th percentiles. * $P < 0.05$ *versus* 1.0 μg/ml propofol.

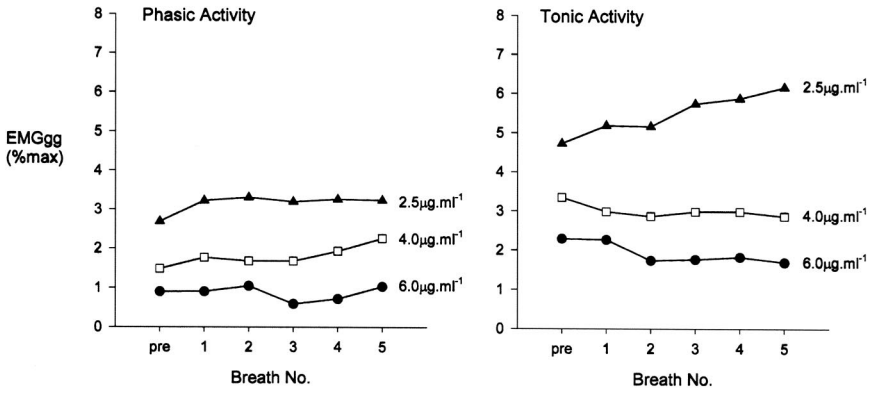

Fig. 6. Effect of decreasing mouth pressure from maintenance levels (pre) to a lower pressure sufficient to cause marked inspiratory flow limitation for five successive breaths (1–5) on the amplitude of phasic and tonic genioglossus electromyogram (EMGgg) activity at each of the three levels of propofol anesthesia. Median values are shown.

Mechanisms of Upper Airway Obstruction during Propofol Anesthesia

In this study, we chose to investigate pharyngeal function related to effect site (brain and, presumably, pharyngeal) propofol concentration. In addition to effect site concentration, in a subgroup of subjects, anesthetic depth was recorded using the Bispectral Index, changes in which paralleled changes in calculated effect site concentration (fig. 3).

At each level of anesthesia, upper airway patency was maintained by CPAP applied *via* a tight-fitting nasal mask. In our subjects, a maintenance CPAP of 12 ± 1 cm H_2O was sufficient to ensure no inspiratory flow limitation.[17] This maintenance pressure was unchanged throughout the study. Maximum inspiratory flow progressively decreased with increasing anesthetic depth (fig. 3), indicating inhibitory effects on central drive to the respiratory pump muscles.[20,21]

The effect of increasing depth of anesthesia on central respiratory output was also reflected in the magnitude of phasic inspiratory EMGgg, which systematically decreased while subjects breathed at a constant maintenance level of CPAP (fig. 5). The magnitude of depression of EMGgg activity with increasing propofol concentration was substantial, being 11% of maximum at subanesthetic concentrations and less than 1% of maximum at a propofol concentration of 6.0 μg/ml. It is likely, however, that these measures *overestimate* EMGgg activity because they were referenced to the maximum activity achieved during voluntary maneuvers while the subject was sedated but able to readily obey commands. Under this condition, even though there was strong encouragement to maximize effort and apparent compliance by the subject, it is probable that voluntary efforts such as tongue protrusion or swallowing, which are known to produce maximal EMGgg activity in conscious subjects, were submaximal.

To our knowledge, this is the first report of a dose-dependent decrease in genioglossus activity with increasing depth of propofol anesthesia in humans. Although our findings are consistent with studies in cats showing dose-dependent decreases in EMGgg[3] and hypoglossal nerve activity[2] during halothane anesthesia, they contrast with our previous findings in humans during isoflurane anesthesia, which showed that phasic inspiratory EMGgg activity was rarely observed, even at very light levels of anesthesia.[6] These contrasting results suggest important interagent differences in pharmacologic properties as well as between-species differences.

The presence of phasic EMGgg activity observed in this study at the deepest levels of propofol, although small in magnitude, contrasts with the abolition of such activity during isoflurane anesthesia.[6] This difference most likely relates to the differential inhibitory effects of these two agents on neural drive to the genioglossus muscle. Potential sources of such inhibition are the inhibitory neurotransmitters γ-aminobutyric acid (GABA) and glycine. Both GABA and glycine immunoreactive neurons are present in the hypoglossal motor nucleus.[22] Glycine and GABA are also released together onto hypoglossal motoneurons, with individual motoneurons containing receptors for both transmitters.[23] Together, their effects are additive in suppressing genioglossus muscle activity.[24] Because propofol works primarily *via* the GABA receptor[25,26] and isoflurane works *via* both the glycine and GABA receptors,[27] it might be expected that isoflurane has a more profound inhibitory effect on genioglossus muscle activity than propofol. However, this is speculative because the interaction between these different pathways and agents on activation of the genioglossus are currently incompletely understood.

In addition to its central effects on respiratory activity, propofol could also influence upper airway muscle activity by inhibiting peripheral reflex pathways. Pressure-sensitive mechanoreceptors located throughout the upper airway cause reflex activation of the genioglossus muscle in a dose-dependent fashion as intraluminal pressure becomes progressively more negative.[28] These reflexes are largely responsible for breath-by-breath changes in phasic EMGgg during normal breathing and for the genioglossus response to inspiratory efforts against an occluded airway.[29,30] We examined the effect of propofol anesthesia on these reflexes by noting the EMGgg response to five successive breaths after a decrease in mask pressure to a level close to Pcrit. Under these conditions of severe flow limitation, successive

inspiratory efforts would normally be accompanied by a progressive increase in phasic genioglossus EMG,[30] the response being mediated principally by activation of pressure-sensitive mechanoreceptors in the upper airway.[31] Such a response was not observed at any level of anesthesia (fig. 6), demonstrating that propofol has a strong inhibitory effect on upper airway mechanoreceptor activity. The observation that tonic activity tended to increase with successive inspiratory efforts at 2.5 μg/ml but not at 4.0 or 6.0 μg/ml suggests that central reflex responses, possibly chemosensory in origin (*e.g.*, to carbon dioxide accumulation during the sequences of flow-limited breaths[32]), may be present at lighter but not at deeper levels of propofol anesthesia. It is, however, important to note that the magnitude of any such response is extremely small and that the magnitude of depression of both tonic and phasic activity is profound and most probably underestimated (see Mechanisms of Upper Airway Obstruction during Propofol Anesthesia, third paragraph).

In contrast to the dose-related decrease in phasic EMGgg observed while subjects breathed at a constant level of CPAP, tonic EMGgg was unaffected by depth of propofol anesthesia. On first inspection, this finding suggests that the basal tone of the upper airway is resistant to the inhibitory effects of propofol on upper airway musculature. However, because tonic activity was defined as the difference between electrical zero and end-expiratory activity, its measurement also consists of a constant level of background electrical noise. It is therefore probable that that true magnitude of tonic activity is lower than that reported in this study. Furthermore, because EMGgg was not measured before administration of propofol, it is possible that tonic EMGgg activity decreased markedly from wakefulness to subanesthetic levels. Such a finding would imply that propofol has a greater effect on tonic than phasic EMGgg activity. These possibilities remain speculative, requiring further investigations incorporating waking measures of genioglossus muscle activity.

In this study, CPAP was used to maintain airway patency and was reduced to provoke transient airflow limitation. It is possible that CPAP influenced phasic EMGgg and upper airway collapsibility by inhibiting pressure-sensitive mechanoreceptors and thereby decreasing EMGgg activity.[33] However, this mechanism is an unsatisfactory explanation for the abolition of an EMGgg response to five successive flow limited breaths, because previous studies have shown that EMGgg activity progressively returns after the first breath after removal of CPAP.[16]

Anesthesia-induced changes in lung volume could also contribute to the observed changes in EMGgg activity and upper airway collapsibility. It is likely that, as propofol concentration and depth of anesthesia increased, lung volume systematically decreased.[34] Such a decrease in lung volume could decrease vagally mediated inhibitory lung inflation reflexes and increase upper airway muscle activity,[35] thereby decreasing upper airway collapsibility. Alternatively, an anesthesia-induced decrease in lung volume could result in increased upper airway collapsibility by virtue of a decreased caudal traction on the upper airway and longitudinal tension within the airway wall.[36–38]

In summary, this study demonstrates that increasing depth of propofol anesthesia is associated with increased collapsibility of the upper airway. This was associated with a profound inhibition of activity of the genioglossus muscle, the major dilator muscle of the upper airway. It seems that this dose-related inhibition is the combined result of depressed central respiratory output to upper airway dilator muscles and depressed upper airway reflexes with these effects both more apparent with increasing depth of anesthesia.

Propofol Anesthesia: Conditions for Study of the Upper Airway with Minimal Neurogenic Influences

To study the mechanical properties of the upper airway, is it critical that potentially confounding neurogenic influences (pharyngeal muscle activity) be controlled or eliminated. Such influences have bedeviled studies of upper airway function during sleep, which are often accompanied by measurement-related changes in variables that affect upper airway stability. For example, the application of nasal CPAP during sleep has been shown to cause relative upper airway muscle hypotonia,[33] which persists for the breath after a reduction in nasal pressure.[39] However, succeeding breaths are accompanied by a progressive return of upper airway muscle activity,[16] limiting this technique to study of the first breath only, an important limitation given the breath-by-breath changes in collapsibility that we and others[6,16,40] have observed.

Furthermore, studies in sleeping subjects are commonly complicated by intermittent arousal and changes in sleep state with accompanying changes in pharyngeal muscle activity. These changes can be precipitated by the measurement technique being used during such studies. Study of the passive upper airway during complete neuromuscular blockade under general anesthesia[41] is also limited because this technique abolishes respiratory as well as pharyngeal muscle activity. Younes *et al.*[42] have clearly shown that measurement of collapsibility under such static conditions underestimates the vulnerability of the upper airway to collapse during physiologic dynamic conditions (*i.e.*, in the presence of airflow).

The current study shows that it is possible to use intravenous propofol anesthesia to minimize neuromuscular activity of the pharyngeal muscles in the presence of continuing activity of the respiratory pump muscles. This provides ideal conditions for the study of mechan-

ical behavior of the hypotonic human upper airway. It has advantages over previous techniques because it permits study of the hypotonic pharynx (1) over many breaths, (2) in the presence of natural decreases in intrapharyngeal pressures generated by spontaneous inspiratory muscle activity, and (3) without the occurrence of state changes.

We have previously administered inhalational anesthesia (isoflurane) *via* the same breathing circuit as used in the current study to obtain measurements of upper airway collapsibility in the absence of neurogenic influences.[6,8] The use of intravenous propofol offers several advantages over this methodology, including the ability to (1) separate the anesthetic delivery system (intravenous) from the measurement system (airway), (2) use a single agent for induction and maintenance of anesthesia, and (3) "titrate" between stable subanesthetic and surgical anesthetic levels.

These properties suggest that study of the upper airway under propofol anesthesia would facilitate, *inter alia*, investigation of the effects on its behavior of mechanical influences, such as changes in head/neck posture, jaw position, and lung volume. Such information would be applicable to both the anesthesia and sleep medicine domains.

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