HIGHLIGHTED TOPIC | Physiology and Pathophysiology of Sleep Apnea

Mandibular advancement decreases pressures in the tissues surrounding the upper airway in rabbits

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Kairaitis, Kristina, Rosie Stavrinou, Radha Parikh, John R. Wheatley, and Terence C. Amis. Mandibular advancement decreases pressures in the tissues surrounding the upper airway in rabbits. J Appl Physiol 100: 349–356, 2006. First published August 25, 2005; doi:10.1152/japplphysiol.00560.2005.—The pharyngeal airway can be considered as an airway luminal shape formed by surrounding tissues, contained within a bony enclosure formed by the mandible, skull base, and cervical vertebrae. Mandibular advancement (MA), a therapy for obstructive sleep apnea, is thought to increase the size of this bony enclosure and to decrease the pressure in the upper airway extraluminal tissue space (ETP). We examined the effect of MA on upper airway airflow resistance (Rua) and ETP in a rabbit model. We studied 11 male, supine, anesthetized, spontaneously breathing New Zealand White rabbits in which ETP was measured via pressure transducer-tipped catheters inserted into the tissues surrounding the lateral (ETPlat) and anterior (ETPant) pharyngeal walls. Airflow, measured via surgically inserted pneumotachograph in series with the trachea, and tracheal pressure were recorded while graded MA at 75° and 100° to the horizontal was performed using an external traction device. Data were analyzed using a linear mixed-effects statistical model. We found that MA at 100° increased mouth opening from 4.7 ± 0.4 to 6.6 ± 0.4 (SE) mm (n = 7; P < 0.004), whereas mouth opening did not change from baseline (4.0 ± 0.2 mm) with MA at 75°. MA at both 75° and 100° decreased mean ETPlat and ETPant by ~0.1 cmH2O/mm MA (n = 7–11; all P < 0.0005). However, the fall in Rua (measured at 20 ml/s) with MA was greater for MA at 75° (~0.03 mmH2O·ml⁻¹·s⁻¹·mm⁻¹) than at 100° (~0.01 mmH2O·ml⁻¹·s⁻¹·mm⁻¹; P < 0.02). From these findings, we conclude that MA decreases ETP and is more effective in reducing Rua without mouth opening.

upper airway extraluminal tissue pressure; upper airway patency

ANTERIOR ADVANCEMENT OF THE mandible has been used to relieve acute upper airway obstruction in unconscious patients for many years (29). More recently, there has been growing interest in using mandibular advancement (MA), achieved most commonly using intraoral devices (referred to collectively as MA splints), to prevent the upper airway narrowing and collapse that occur in obstructive sleep apnea (OSA) patients during sleep (3, 16, 20). However, the effectiveness of this therapeutic approach has been highly variable with a recent randomized controlled study reporting reduction of apnea-hypopnea index (AHI) to <5 events/h in only ~37% of OSA patients (8, 20).

MA has been shown to increase pharyngeal cross-sectional area in anesthetized (12) and awake human subjects (9), as well as to decrease upper airway resistance (Rua) in awake human subjects (17) and to decrease upper airway closing pressures in sleeping OSA patients (21). However, there has been poor understanding of the mechanisms by which MA improves upper airway patency or, at least, reduces upper airway collapsibility. Previous workers have suggested that MA may improve upper airway patency via an increase in genioglossus muscle activity (1), a decrease in upper airway extraluminal tissue pressure (ETP) (12), or traction on the lateral pharyngeal walls caused by anterior displacement of the tongue (12). However, because MA can improve upper airway patency during muscle paralysis (12), increased upper airway muscle activity is unlikely to be an exclusive mechanism.

Although it is widely understood that the patency of the pharyngeal airway is determined by the ability of the airway walls to resist the collapsing forces generated by negative intraluminal pressures during inspiration, it has been appreciated for more than two decades (27) that pharyngeal airway muscle activity is also impacted by the pressure existing in the peripharyngeal tissues. Despite this awareness, there have been few studies that have measured ETP. The first measurements of ETP were made in pigs by Winter et al. (38, 39) almost a decade ago. More recently, our laboratory has measured ETP in an anesthetized rabbit model and shown that ETP is usually positive (thus exerting a collapsing pressure on the pharyngeal airway), fluctuates with respiration, and is increased by mechanical influences such as head and neck flexion (14). The precise determinants of ETP remain unclear, but it has been suggested that the boundary conditions that define the upper airway extraluminal tissue space may play a role (34, 37).

Although usually modeled as a floppy-walled tube, the upper airway can also be considered as a luminal shape formed by the surrounding tissues. In turn, these tissues are partially enclosed within a bony box subtended by the mandible, skull, and cervical spine. In this model, the ETP may be influenced by the mechanical influences such as head and neck flexion (14). The precise determinants of ETP remain unclear, but it has been suggested that the boundary conditions that define the upper airway extraluminal tissue space may play a role (34, 37).

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determinant of the bony box volume and, hence, may alter the transmural pressure operating across the pharyngeal wall through an effect on ETP.

To explore the hypothesis that MA may improve upper airway patency, at least in part, via a reduction in ETP, we utilized an established animal model to examine relationships between MA, pharyngeal ETP, and upper airway patency.

**METHODS**

**Animals.** Studies were performed in 11 adult supine male New Zealand White rabbits (2.5–3.6 kg). The protocol was approved by the Western Sydney Area Health Service Animal Ethics Committee.

**Anesthesia.** Anesthesia was induced with an intramuscular injection of ketamine (35 mg/kg) and xylazine (5 mg/kg) and maintained using intravenous ketamine (15 mg·kg⁻¹·h⁻¹) and xylazine (4.5 mg·kg⁻¹·h⁻¹).

**Upper airway airflow, tidal volume, and tracheal pressure.** Tracheal pressure (Ptr) and upper airway airflow (V) were monitored using a pressure transducer (±10 cmH₂O; Celesco, Chatsworth, CA) and heated pneumotachograph (model 8300A, Hans Rudolph, Kansas, MO), respectively, both inserted in series between the third and tenth cartilage rings of the intact trachea (Fig. 1). Tidal volume (Vt) was obtained via electrical integration of the V signal.

**Measurement of ETP.** Pharyngeal ETP was measured using pressure transducer-tipped catheters (Millar MPC 500, Millar Instruments, Houston, TX) surgically inserted into the tissues surrounding the pharyngeal airway as previously described (14). Briefly, pressure was measured in the pharyngeal submucosal tissues at the level of the angle of the mandible for 1) the right lateral pharyngeal wall ETP (ETPlat) and 2) the anterior pharyngeal wall ETP (ETPant) midline in the coronal plane. Correct positioning of each catheter was verified via postmortem dissection at the conclusion of each study.

**MA.** Head and neck position were controlled at 50° to the horizontal relative to a line drawn from the tragus to the external nare. The lower incisor teeth were removed, and an 0 silk suture was passed around the mandibular symphysis. The suture thread was attached to a specially designed external MA device fitted with a screw via which graded tension could be applied to the suture thread and the mandible advanced. MA (0–5 mm in 1-mm increments from baseline) and angle of MA [referenced to the horizontal; 75° (n = 11), 85° (n = 7) and 100° (n = 7)] were quantified using an incorporated scale and angle finder. Mouth opening dimension (distance between upper incisor teeth and lower jaw) was also measured at MAs of 0 and 5 mm (Fig. 1).

**Data analysis.** Mean and Δ (the size of the respiratory fluctuations, maximum – minimum) values were obtained for three runs of five steady-state breaths for each condition. Power functions (Ptr = aVᵇ + c, where a, b, and c are constants) were fitted to the inspiratory limb of Ptr/V curves between V = 0 and 20 ml/s (Figs. 2 and 3), and Rua (Ptr/V at inspiratory V = 20 ml/s) was calculated. The presence or absence of V limitation was quantified by visual inspection of the Ptr vs. V plots, and it was said to be present if there was an increase in Ptr in the absence of an increase in inspiratory V.

Individual run data were averaged to obtain individual rabbit data that were then pooled to obtain group mean (±SE) data. All group mean baseline data were compared using a one-way ANOVA, with Bonferroni post hoc correction. P < 0.01 was considered significant.

A linear mixed-effects model (25) was used to examine the individual rabbit (random effect) interactions between MA (fixed effect), advancement angle (fixed effect), Rua (fixed effect), and ETP values anteriorly and laterally (fixed effect). Relationships between the change in mean ETP from baseline with both MA (fixed effect) and Rua (expressed as a percentage of baseline Rua, fixed effect), at each angle of MA (fixed effect), were also examined within individual rabbits (random effect) at each catheter position. P < 0.05 was considered significant.

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**Table 1. Grouped data at baseline before the mandibular advancement, at each of the mandibular advancement angles of 75, 85, and 100° for distance between the upper incisor teeth and mandibular symphysis, tidal volume, upper airway resistance, and mean lateral and anterior extraluminal tissue pressure**

<table>
<thead>
<tr>
<th>Angle of MA</th>
<th>75° (n = 11)</th>
<th>85° (n = 7)</th>
<th>100° (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth opening, mm</td>
<td>4.0 ± 0.2</td>
<td>4.1 ± 0.4</td>
<td>4.7 ± 0.4</td>
</tr>
<tr>
<td>Vt, ml</td>
<td>15.4 ± 2.0</td>
<td>16.0 ± 3.9</td>
<td>16.0 ± 3.8</td>
</tr>
<tr>
<td>Rua, mmH₂O/ml⁻¹·s</td>
<td>0.6 ± 0.1</td>
<td>0.44 ± 0.0</td>
<td>0.46 ± 0.0</td>
</tr>
<tr>
<td>ETPlat, cmH₂O</td>
<td>1.8 ± 0.7*</td>
<td>0.6 ± 0.6*</td>
<td>0.9 ± 0.5*</td>
</tr>
<tr>
<td>Δ</td>
<td>0.6 ± 0.0</td>
<td>0.5 ± 0.0</td>
<td>0.6 ± 0.0</td>
</tr>
<tr>
<td>ETPant, cmH₂O</td>
<td>0.7 ± 0.5</td>
<td>0.3 ± 0.5</td>
<td>0.2 ± 0.5</td>
</tr>
<tr>
<td>Δ</td>
<td>0.6 ± 0.0</td>
<td>0.5 ± 0.0</td>
<td>0.5 ± 0.0</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of animals. Mouth opening, distance between upper incisor teeth and mandibular symphysis; VT, tidal volume; Rua, upper airway resistance; ETPant, anterior pharyngeal wall extraluminal tissue pressure; ETPlat, lateral pharyngeal wall extraluminal tissue pressure; Δ, size of respiratory fluctuations (maximum – minimum). There were no significant differences between the baseline values for any of the protocols compared with the other baseline values (all P > 0.05). However, mean ETPlat was greater than mean ETPant for all mandibular advancement angles by −0.7 cmH₂O (*P < 0.003 compared with ETPant).
RESULTS

There were no significant differences in the group mean baseline values for Vt, mouth opening dimension, Rua, and all ETP measures that were obtained immediately before the commencement of MA for each angle of advancement tested (Table 1). However, for all angles of MA, baseline ETPlat values were significantly greater than the corresponding ETPant values by \( \sim 0.7 \) cm H2O \( (P < 0.003; \text{Table 1}) \). For the group, MA at all angles resulted in a fall in ETPlat and ETPant (Fig. 2), and it was associated with a reduction in Rua (Fig. 3).

Positioning of Millar catheters. Postmortem examination revealed pressure transducer-tipped catheters were located in the submucosa of the peripharyngeal tissues in all but two rabbits. In both of these rabbits, the anterior catheter was located in the tissues immediately below the tissues surrounding the pharynx. However, data were still included in the analysis because the results were not substantially different from other data for ETPant.

Effect of MA on Vt. When the mandible was advanced to 5 mm, at 75° the Vt was 16.7 \( \pm 2.2 \) ml, at 85° it was 16.1 \( \pm 4.0 \) ml, and at 100° it was 15.7 \( \pm 3.6 \) ml (all not significantly different from baseline value, \( P > 0.4 \)).

Effect of MA on mouth opening. When 5 mm of MA at 75° were applied, there was no significant increase in the measured mouth-opening dimension from the resting value of 4.0 \( \pm 0.2 \) mm. However, mouth opening increased to 5.7 \( \pm 0.6 \) mm at 85° and 6.6 \( \pm 0.4 \) mm at 100° (both \( P < 0.004 \)).

Effect of MA on V limitation. For a MA angle of 75°, from inspection of the Ptr vs. V plots, inspiratory V limitation (see Fig. 3) was present at baseline in 4 of 11 rabbits, was present at 1 and 2 mm of advancement in 3 of 11 rabbits, and was absent at all levels of MA \( > 2 \) mm. For MA angles of both 85 and 100°, flow limitation was present in one of seven rabbits at both baseline and at 1 mm, and it was absent at all levels of advancement \( > 1 \) mm.

Effect of MA on Rua. Graded MA, across all angles, resulted in a 0.01- to 0.03-mm H2O\( \cdot \)ml\(^{-1}\)\( \cdot \)s\(^{-1}\) decrease in Rua (Figs. 4A and 5A). However, the rate of fall for Rua was significantly greater at an MA of 75° than at 85° or 100° \( (P < 0.01 \text{ compared with MA 85° and 100°}; \text{Fig. 5A}) \).

Effect of MA on ETP. During graded MA, mean ETPlat, mean ETPant, and \( \Delta \)ETPlat all fell progressively at all MA angles (Table 2, Figs. 4B and 5B). When the data were examined using the linear mixed-effects model, for every 1 mm of MA, both group mean ETPlat and mean ETPant fell by \( \sim 0.1 \) cm H2O (both \( P < 0.01; \text{Table 2, Fig. 5B}) \). The only change in \( \Delta \)ETP with MA was a decrease in ETPlat at an MA angle of 75° (Table 2, Fig. 5C).
Relationships between Rua and ETP during MA. For the group, there was a significant relationship between the change in mean ETPlat and ETPant (from baseline) during MA and the Rua (expressed as percentage of baseline Rua) for all angles of MA (all \( P < 0.0001 \), Fig. 6). For mean ETPlat, there was a significant interaction with angle of MA in that there was a greater fall in Rua per unit decrease in mean ETPlat with MA at 75° than at the other angles (\( P < 0.01 \) compared with 85° and 100°; Fig. 6).

**DISCUSSION**

This study demonstrated that in an anesthetized rabbit model increasing MA resulted in both a decrease in the pressures in the tissues surrounding the upper airway and a decrease in Rua. Furthermore, there was a significant linear relationship between the decrease in ETP achieved with MA and the decrease in Rua. However, the rate of fall in Rua with MA was greater if the angle of advancement (75°) was such that mouth opening did not occur. These findings are the first to demonstrate changes in ETP with MA. Our results support the notion that MA may, at least in part, influence upper airway patency through a fall in ETP.

**Critique of methods.** Anesthetized rabbits have been used previously in a number of physiological studies of upper airway mechanics (15, 19, 24), and our laboratory has also employed this model to investigate the mechanics of the upper airway extraluminal tissue space (14). General anesthesia depresses upper airway muscle activity (7, 22, 23), producing a physiological model similar to sleep (6). In the present study, upper airway muscle activity was not monitored; thus it is possible our results may have been influenced by upper airway muscle recruitment. However, using the same anesthetic regime in a feline upper airway model, other workers have demonstrated quiescent upper airway muscles during tidal

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Fig. 4. Individual rabbit data showing the effect of graded MA at an angle of 75° on change from baseline in Rua (ΔRua: A), mean ETPlat (ΔMean ETPlat: B), and mean ETPant (ΔMean ETPant: C). Individual rabbits are represented by different symbols.

Fig. 5. Fitted linear functions obtained from the data for all rabbits using the linear mixed-effects model for Rua (Δ), mean ETPlat and ETPant (B), and ΔETPlat (C) for MA angles of 75° (solid line), 85° (dotted line), and 100° (dashed line). All line slopes shown are significant at \( P < 0.01 \). *\( P < 0.01 \) compared with 85° and 100°. Note that no significant slope was obtained for ΔETPant.
come tested in the present study is likely to be primarily related mainly influenced by airway dimensions (35). Thus the out-
graded MA. As an index of upper airway patency, Rua is
with V˙ limitation, as a marker of the functional outcome of

A

values for slopes obtained using the linear mixed-effects model at each of the angles of mandibular advancement showing the effect of mandibular advancement on Δ and mean ETPlat and ETPant and Rua

<table>
<thead>
<tr>
<th></th>
<th>MA 75°</th>
<th>MA 85°</th>
<th>MA 100°</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Slope</td>
<td>SE</td>
<td>t</td>
</tr>
<tr>
<td>ETPant, cmH2O/mm MA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>−0.10</td>
<td>0.03</td>
<td>−4.1</td>
</tr>
<tr>
<td>Δ</td>
<td>−0.01</td>
<td>0.0</td>
<td>−2.5</td>
</tr>
<tr>
<td>ETPant, cmH2O/mm MA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>−0.10</td>
<td>0.02</td>
<td>−6.5</td>
</tr>
<tr>
<td>Δ</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rua, mmH2O·mm−1·s·mm MA−1</td>
<td>−0.03*</td>
<td>0.0</td>
<td>−6.7</td>
</tr>
</tbody>
</table>

Values are means ± SE. MA, mandibular advancement; NS, nonsignificant slope. Degrees of freedom = 134 for all values. All values for the slopes are significant (P < 0.01). *P < 0.05 compared with MA at 85 and 100°.

to mandibular effects on upper airway geometry, rather than on the collapsibility of upper airway walls. However, some insight into effects on wall collapsibility may be gleaned by an examination of the effect of MA on the prevalence of inspiratory V-limited breaths. Inspiratory V limitation was present at baseline in some rabbits, but it was abolished by MA in all cases, suggesting reduced upper airway wall collapsibility.

The effect of MA on the rabbit upper airway has not previously been reported. Although our rabbit model is not intended to act as a model of OSA, rabbits are naturally retrognathic, and in humans retrognathia and reduced mandibular length are recognized causes of OSA (4, 11, 18). Consequently, the rabbit may be suited to studies that assess the mechanical consequences of mandibular geometry.

In our experimental design, we have chosen to use an external traction device to advance the mandible, and this differs from intraoral MA splints. It is possible that there are differences in the effect of an intraoral device compared with external traction, due perhaps to stimulation of mechanoreceptors; however, because our rabbits are anesthetized, these reflexes are likely to be suppressed. In addition, MA with intraoral splints is achieved not by graded advancement as performed here but via advancement to one level. This may have a different effect on the upper airway than graded ad-
vancement. The external traction device allowed us to vary the angle at which we advanced the mandible. Different angles of advancement have not been reported for MA splints; however, controversy exists over the degree of mouth opening that should occur with MA. Some authors report greater improvements in AHI with MA splints when mouth opening was promoted (3, 16), although a recent randomized crossover trial reported no difference in outcomes between two devices, one with and one without mouth opening (26). In our study, varying the angle of advancement was employed as a methodology for producing varying degrees of mouth opening.

The limitations of the methodology for measuring ETP have been discussed previously (14, 38, 39). Briefly, the surgical insertion of the catheter and the space occupying nature of the catheter will both result in a perturbation of the baseline ETP. For this reason, most of our analyses are based on comparisons of the change from baseline, rather than absolute values. ETP was chosen as an outcome variable rather than the transmural pressure (the pressure acting across the upper airway walls, which is the difference between intraluminal and extraluminal pressures), because the upper airway was intact and there was

Fig. 6. Linear mixed-effects model showing relationships obtained during MA at 75° (line), 85° (dashed line) and 100° (dotted line) between Rua (% of baseline Rua) and change from baseline for mean ETPlat (A) and mean ETPant (B). Note greater decrease in Rua per unit change in mean ETPlat for MA at 75° (A). All slopes are significant at P < 0.0001. *P < 0.01 compared with 85 and 100°.
airflow through the upper airway. Measurement of $P_{tr}$, in the presence of airflow, will not be reflective of the luminal pressure acting at the site of the measurement of ETP. Depending on the flow regime, even an intraluminal pressure catheter present at the same level as the catheters measuring ETP may not reflect the intraluminal pressure acting at the luminal mucosa.

**Baseline ETP.** Baseline values for all ETP measures were not significantly different for the different advancement angles used and were similar to those our laboratory has reported previously for anesthetized rabbits (14). Values for $ETP_{lat}$ were consistently greater than those for $ETP_{ant}$ by $\sim 0.7 \text{ cmH}_2\text{O}$. This finding is also similar to our laboratory’s previous data (14) and demonstrates that ETP is not uniformly distributed around the pharyngeal airway. A positive ETP will exert a collapsing pressure on the upper airway. For the airway to remain patent, an “upper airway dilating pressure” (e.g., elastic recoil, dilator muscle activity) equal and opposite to the ETP must be present. When upper airway dilator muscle activity is depressed, this force is presumably associated with the elastic properties of the upper airway wall (outward recoil). Some insight into the effect of MA on this upper airway dilating pressure may be gained by considering the ETP values at the zero-flow points during tidal breathing in the present study. With no airflow, intraluminal pressure in an open upper airway is atmospheric and transmural pressure is equivalent to ETP. Moreover, if the airway wall is not in motion, then upper airway dilating pressure is equal and opposite to ETP. In the present study, ETP (no airflow) fell with progressive MA (see Fig. 2), implying that upper airway dilating pressure also fell. In this scenario, MA lowers ETP, thus reducing transmural compression of the airway and promoting attainment of a new equilibrium point characterized by increased luminal dimensions (as evidenced by reduced $R_{ua}$) and reduced upper airway-dilating pressure, which in the absence of dilator muscle activity, likely represents reduced outward “wall recoil pressure.”

We also recorded, as has been reported previously by other workers and our laboratory (14, 38, 39), negative values for ETP. If the ETP is negative, it will be exerting a force that will tend to hold the upper airway open. ETP is the total tissue pressure acting at the point, and it is the sum of the pressures exerted by the solid and fluid elements of the tissues, or the solid tissue pressure and the interstitial fluid pressure (10). The presence of a negative pressure in the tissues may be because we have reduced the pressure exerted by the solid elements, through tissue movement as the bony enclosure expands, and are thus predominantly measuring the pressure exerted by the interstitial fluid, which is reported to be negative (10).

**MA and ETP.** The present study is the first to combine measurement of ETP with graded MA. Our findings clearly demonstrate that both $ETP_{ant}$ and $ETP_{lat}$ are progressively reduced during MA. However, the rate of decrease in all measures of ETP was not significantly influenced by measurement site or angle of advancement. Thus, although ETP is nonuniformly distributed around the pharyngeal airway, the relative effect of MA on these pressures is homogeneous. The sole exception was that $ETP_{lat}$ decreased significantly with increasing MA only when the advancement angle was $75^\circ$; i.e., the $ETP_{lat}$ fluctuations associated with the respiratory cycle became increasingly damped, and this effect was influenced by both measurement site and angle of advancement.

Because measured ETP values were mostly above atmospheric pressure, a decrease in ETP reduces the compressive pressure being exerted on the pharyngeal airway walls, i.e., alters transmural pressure. Although the magnitude of the falls in ETP were small in absolute terms (<0.5 cmH$_2$O), the functional effect of this on airway patency will depend on the collapsibility of the airway wall. If airway walls are highly compliant or, inspiratory luminal pressure is close to upper airway closing pressure, a change in ETP of the magnitude demonstrated in the present study may be sufficient to prevent airway closure.

**Relationship between $R_{ua}$ and ETP.** During MA, we found significant linear relationships between both $\Delta ETP_{lat}$ and $\Delta ETP_{ant}$ and $\Delta R_{ua}$ (Fig. 6). This finding, although not definitive, is consistent with the contention that the effect of MA on upper airway patency may be mediated via its effect on ETP. However, an intriguing finding emerged for MA at $75^\circ$. For this angle alone, the rate of fall in $R_{ua}$ per unit fall in mean $ETP_{lat}$, but not $ETP_{ant}$, was significantly greater than for the other angles (Fig. 6A). Because the rate of reduction of $ETP_{lat}$ with MA was the same at all angles (Fig. 5), this finding suggests that there is an angle of advancement interaction

![Figure 7](http://example.com/figure7.png)
between the change in ETPlat and the change in Rua and, furthermore, that this does not apply to ETPant; i.e., Rua is more sensitive to changes in ETPlat than ETPant but only when the advancement angle is 75°. Because mouth opening occurred with MA of 85 and 100°, there was potential for leakage of airflow via the mouth (potential low-resistance pathway) to influence the results. However, mouth leak is unlikely to have occurred because overlap of the epiglottis and soft palate is a normal characteristic of rabbit upper airway anatomy. Furthermore, the rate of fall of Rua with MA was greatest at a MA angle (75°) that did not result in mouth opening. A potential explanation may lie in effects of mouth opening on lateral pharyngeal wall compliance, which is the radial displacement that occurs in response to a change in intraluminal pressure.

In this study, MA at 75° resulted in a significant reduction in the size of the respiratory-related fluctuations in ETP in the lateral pharyngeal walls (ΔETPlat), which did not occur at any of the other angles. The magnitude of ΔETP, as discussed previously (14, 38, 39), may be related either to upper airway muscle activity, tracheal traction, or pressure transmission from the upper airway lumen. Because VT is unchanged by MA, it seems unlikely that there has been a change in tracheal traction. It also seems unlikely, because the degree of mouth opening was small, that different upper airway muscle activation or different vector action of upper muscles has occurred with such small changes in MA; however, this remains a possibility. Alternatively, there may have been a small decrease in the intraluminal pressures transmitted across the lateral pharyngeal walls. This may reflect decreased intraluminal pressure fluctuations associated with a decreased Rua, but that should have influenced both ΔETPlat and ΔETPant. Intraluminal pressure transmission is likely to occur through movement of the upper airway walls, which has been demonstrated during tidal breathing in human subjects (31, 30). Thus we speculate that this result may reflect decreased compliance of the lateral pharyngeal walls, perhaps associated with mucosal unfolding during MA at 75°. If this is correct then reduced lateral wall compliance may have contributed to the observed greater rate of fall of Rua with MA at 75°. In support of this, upper airway collapsibility (measured by critical closing pressure) in sedated (midazolam) human subjects increased with increasing mouth opening, with no change in upstream resistance (2). A similar model, where upper airway patenty is determined by both wall compliance and ETP, has been proposed to explain the effect of tracheal traction on upper airway patenty in the cat (28, 32).

Proposed model of MA. Recently, Watanabe and colleagues (34) proposed a model of the upper airway as an airway lumen surrounded by tissues constrained within a bony box formed by the spine and mandible. These workers suggested that pharyngeal airway patency was influenced by the pressure in the box-enclosed tissues and that this pressure would depend on the relative (unrestrained) volumes of tissues and bony box. Using their model an increase in box volume should be associated with a fall in the pressure in the tissues. The fall in ETP with MA in the present study is consistent with this view. MA may exert an effect on upper airway patency via an ETP-lowering increase in bony box volume.

The single-compartment model of Watanabe and colleagues (34), however, is not consistent with the ETP heterogeneity demonstrated in our present and previous studies. In general we find that, in anesthetized rabbits, ETPlat is ~0.7 cmH2O greater than ETPant (14), suggesting structural and/or functional compartmentalization in the periphery. In Fig. 7, we present a modified version of the model of Watanabe et al. that includes functional anterior and lateral ETP compartments. In the two-dimensional model proposed by Watanabe et al. the bony enclosure is represented as a square or circular container (34). We have represented the bony enclosure as a triangle, because this is more reflective of mandibular anatomy. Anterior movement of the triangular-shaped mandible would result in an increase in both the lateral and anterior dimensions of the bony enclosure of the upper airway (see Fig. 7). In our proposed model, to the extent that the anterior and lateral ETP compartments are functionally independent, MA reduces ETPlat primarily as a result of an increase box lateral dimensions as the wider part of the mandible moves anteriorly, whereas the reduction in ETPlat results from the increase in the anteroposterior dimension of the box as the mandible is moved anteriorly (see Fig. 7).

In conclusion, we have demonstrated that in an anesthetized rabbit model, both Rua and ETPlat fall with MA. The decreases in Rua that occur with MA are linearly related to the fall in ETPlat with MA. We hypothesize that the Rua changes with MA are mediated via the changes in ETP, especially the changes in ETPlat, which in turn results in an alteration in the transmural pressure acting across the upper airway wall. In addition, we speculate that MA without mouth opening results in a reduction in upper airway wall compliance, which does not occur when the mouth is opened. Our findings are consistent with the hypothesis that MA exerts, at least in part, an effect on upper airway patency through an expansion of the boundary conditions that define the pharyngeal airway extraluminal tissue space.

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